

(19)

Europäisches Patentamt
European Patent Office
Office européen des brevets



(11)

EP 1 227 152 A1

(12)

EUROPEAN PATENT APPLICATION

(43) Date of publication:
31.07.2002 Bulletin 2002/31

(21) Application number: 01102050.0

(22) Date of filing: 30.01.2001

(51) Int Cl.7: C12N 15/31, C12N 1/20,
C07K 14/195, C07K 16/12,
C12Q 1/68, A61K 39/02,
G01N 33/53, G06F 19/00,
C12R 1/01
// (C12N1/20, C12R1:01)

(84) Designated Contracting States:
AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU
MC NL PT SE TR
Designated Extension States:
AL LT LV MK RO SI

(74) Representative: Becker Kurig Straus
Patentanwälte
Bavariastrasse 7
80336 München (DE)

Remarks:

- The biological material has been deposited with CNCM under number(s) I-2618
- The sequence listing, which is published as annex to the application documents, was filed after the date of filing. The applicant has declared that it does not include matter which goes beyond the content of the application as filed.

(71) Applicant: Société des Produits Nestlé S.A.
1800 Vevey (CH)

(72) Inventor: The designation of the inventor has not yet been filed

(54) Bacterial strain and genome of bifidobacterium

(57) The present invention pertains to a novel microorganism of the genus *Bifidobacterium* longum, in particular to its genomic sequence and the nucleotide sequences encoding polypeptides of *Bifidobacterium* NCC2705 (CNCM I-2618), which are secreted or specific or which are involved in the metabolism, in the replication process, and to polypeptides encoded by such sequences as well as to vectors including the said sequences and cells or non-human animals transformed with these nucleotide sequences and vectors, respec-

tively. The invention also relates to transcriptional gene products of the *Bifidobacterium* genome and to methods of detecting these nucleic acids or polypeptides. The invention eventually comprises a data carrier comprising the nucleotide sequence and/or polypeptide sequence of NCC2705 and also pertains to food and pharmaceutical compositions containing said microorganism for the prevention and/or treatment of diarrhea brought about by rotaviruses and pathogenic bacteria containing said *Bifidobacterium*.

PATHOGENS SENSITIVITY TO HUMAN BIFIDOBACTERIA NCC 2705

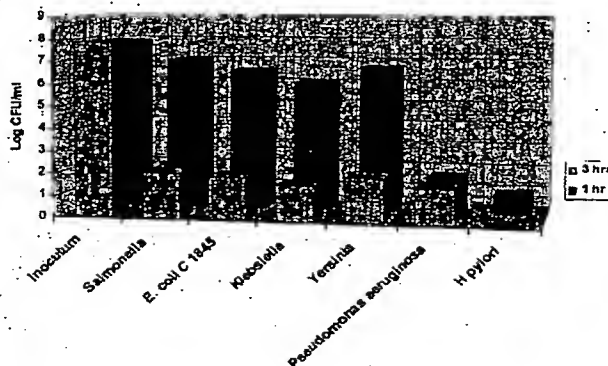


FIG. 2

Description

[0001] The present invention pertains to a novel microorganism of the genus *Bifidobacterium longum*, in particular to its genomic and plasmid sequence and nucleotide sequences encoding polypeptides of said *Bifidobacterium*, to vectors including the said sequences and cells or non-human animals transformed with these nucleotide sequences and vectors, respectively. The invention also relates to transcriptional and translational products of the *Bifidobacterium* genome and to methods of detecting these nucleic acids or polypeptides, respectively. The invention also relates to a data carrier comprising nucleotide sequences and/or polypeptide sequences of NCC2705. In addition, the present invention pertains to the *Bifidobacterium longum* strain NCC2705 and also to food and pharmaceutical compositions containing said *Bifidobacterium* or active components thereof for the prevention and/or treatment of diarrhea brought about by rotaviruses and pathogenic bacteria.

[0002] Organisms that produce lactic acid as a major metabolic component have been known since decades. These bacteria are normally found in milk or in milk processing factories, respectively, living or decaying plants but also in the intestine of man and animals. These microorganisms, summarized under the term "lactic acid bacteria", represent a rather inhomogeneous group and comprise the genera *Lactococcus*, *Lactobacillus*, *Streptococcus*, *Bifidobacterium*, *Pediococcus* etc..

[0003] Lactic acid bacteria have been utilized by mankind as fermenting agents for the preservation of food taking benefit of a low pH and the action of products generated during the fermentative activity thereof to inhibit the growth of spoilage bacteria. In addition, lactic acid bacteria have also been used for preparing a variety of different foodstuff such as cheese, yogurt and other fermented dairy products from milk.

[0004] Quite recently lactic acid bacteria have attracted a great deal of attention in that some strains have been found to exhibit valuable properties to man and animals upon ingestion. In particular, specific strains of the genus *Lactobacillus* or *Bifidobacterium* have been found to pass the gastro-intestinal tract in a viable and live form without getting destroyed in the upper part thereof, especially by the impact of the low pH prevailing in the stomach and be able to colonize the intestinal mucosa, with their temporary or sustained maintenance in the gut being presumed to bring about numerous positive effects on the health of the living beings. These strains are generically termed probiotics.

[0005] EP 0 768 375 discloses such a specific strain of the genus *Bifidobacterium*, that is capable to become implanted in the intestinal flora and may adhere to intestinal cells. This *Bifidobacterium* is reported to assist in immunomodulation, being capable to competitively exclude adhesion of pathogenic bacteria to intestinal cells, thus supporting the maintenance of the individual's health.

[0006] In view of the valuable properties particular strains of lactic acid bacteria may provide, there is a desire in the art for additional lactic acid bacterial strains that are beneficial to the well being of man and/or animal. In addition, a more detailed information is desired relating to the biology of these strains, in particular as regards the interaction with the hosts, the phenomena of passing different environmental conditions in the gut as well as having the capability to adhere to the intestine's mucosa and eventually the involvement in the enhancement of the immune system and defense against pathogens, which information will allow a better understanding of these mechanisms.

[0007] Consequently, a problem of the present invention is to provide substantial data about bacterial strains that exhibit properties beneficial for man and/or animals.

[0008] In view of said problem, a subject of the present invention is the nucleotide sequence having the sequence SEQ. ID. No. 1 of the lactic acid bacterium *Bifidobacterium longum* NCC2705 genome and/or the nucleotide sequence SEQ. ID. No. 1099 of the plasmid contained therein. The invention is, however, not limited to the sequences indicated in SEQ. ID. No. 1 and SEQ. ID. NO. 1099, respectively, but encompasses genomes and nucleotides encoding polypeptides of strain variants, polymorphisms, allelic variants, and mutants thereof.

[0009] In the figures:

Fig. 1 shows a graph, indicating the capability of *Bifidobacterium longum* NCC 2705 to adhere to human intestinal cells in culture; as a comparison another *Bifidobacterium* strain BL28 Ca1 was used;

Fig. 2 shows the pathogen sensitivity of pathogenic bacteria towards *Bifidobacterium longum* NCC2705;

Fig. 3 shows the activity of the cell lines NCC2705 and B1 2B against *S. typhimurium* SL1344 infecting Caco-2 cells;

Fig. 4 shows the rate of survival of mice infected with *Salmonella typhimurium* SL 1344 and treated with the *Bifidobacterium* NCC2705.

Fig. 5 shows a scheme illustrating the cell culture screening for assessing rotaviral protective properties of the bacterial strain NCC 2705.

[0010] The present invention is based on whole-genome sequencing of the genome of the *Bifidobacterium longum* strain NCC 2705, that has been deposited with the Institute Pasteur according to the Budapest Treaty on January 29th, 2001 receiving the deposit no. CNCM I-1-2618.

[0011] In a first aspect the present invention relates to nucleotide sequences selected from the group comprising (a) the nucleotide sequence of SEQ. ID. No. 1; (b) a nucleotide sequence exhibiting at least 90% identity with the sequence of SEQ. ID. No. 1; or (c) a nucleotide sequence that is homologous or hybridizes to SEQ. ID. No. 1 under stringent conditions.

[0012] In another aspect the invention relates to nucleotide sequences selected from the group comprising (a) the nucleotide sequence of SEQ. ID. No. 1099; (b) a nucleotide sequence exhibiting at least 90% identity with the sequence of SEQ. ID. No. 1099; or (c) a nucleotide sequence that is homologous or hybridizes to SEQ. ID. No. 1099 under stringent conditions.

[0013] The terms genome or genomic sequence shall be understood to mean the sequence of the chromosome of *Bifidobacterium longum*. The term plasmid shall be understood to designate any extrachromosomal piece of DNA contained in the *Bifidobacterium* of the present invention. Nucleotide sequence, polynucleotide or nucleic acid are understood to designate a double-stranded DNA, a single-stranded DNA or transcriptional products of the said DNAs at various length including oligonucleotides of about 10 to 100 nucleotides in length.

[0014] A homologous nucleotide sequence according to the present invention is understood to mean a nucleotide sequence having a percentage identity with the bases of the nucleotide sequence SEQ. ID. No. 1 or SEQ. ID. No. 1099 of at least 80%, preferably 90% and more preferably 95%, 96%, 97%, 98% or 99%. The said homologous may comprise, e.g., the sequences corresponding to the genomic sequence or to the sequences of its representative fragments of a bacterium belonging to the *Bifidobacterium* species, preferably the *Bifidobacterium longum* species, as well as the sequences corresponding to the genomic sequence or to the sequences of its representative fragments of a bacterium belonging to the variants of the species *Bifidobacterium*. In the present invention, the terms species and genus are mutually interchangeable.

[0015] These homologous sequences may thus correspond to variations linked to mutations within the same species or between species and may correspond in particular to truncations, substitutions, deletions and/or additions of at least one nucleotide. The said homologous sequences may also correspond to variations linked to the degeneracy of the genetic code or to a bias in the genetic code which is specific to the family, to the species or to the variant and which are likely to be present in *Bifidobacterium*.

[0016] Protein and/or nucleic acid sequence homologies may be evaluated using any of the variety of sequence comparison algorithms and programs known in the art. Such algorithms and programs include, but are by no means limited to, TBLASTN, BLASTP, FASTA, TFASTA, and CLUSTALW (see e.g. Pearson and Lipman, 1988, Proc. Natl. Acad. Sci. USA 85 (8): 2444-2448; Altschul et al., 1990, J. Mol. Biol. 215 (3): 403-410; Thompson et al., 1994, Nucleic Acids Res. 22 (2): 4673-4680; Higgins et al., 1996, Methods Enzymol. 266: 383-402; Altschul et al., 1990, J. Mol. Biol. 215 (3): 403 - 410; Altschul et al., 1993, Nature Genetics 3: 266-272).

[0017] In a particularly preferred embodiment, protein and nucleic acid sequence homologies are evaluated using the Basic Local Alignment Search Tool ("BLAST") which is well known in the art (supra). In particular, four specific BLAST programs have been used to perform the following task:

(1) BLASTP	Compares an amino acid query sequence against a protein sequence database
(2) BLASTN	Compares a nucleotide query sequence against a nucleotide sequence database
(3) BLASTX	Compares a nucleotide query sequence translated in all reading frames against a protein sequence database
(4) TBLASTN	Compares a protein query sequence against a nucleotide sequence database dynamically translated in all reading frames

[0018] Among these representative fragments, those capable of hybridizing under stringent conditions with a nucleotide sequence according to the invention are preferred. Hybridization under stringent conditions means that the temperature and ionic strength conditions are chosen such that they allow hybridization to be maintained between two complementary DNA fragments. Such conditions of high stringency may e.g. be achieved by carrying out the hybridisation at a preferred temperature of 65 °C in the presence of SSC buffer, e.g. 1 x SSC corresponding to 0.15 M NaCl and 0.05 M Na-citrate. The washing steps may be, for example, the following: 2 x SSC, 0.1% SDS at room temperature followed by three washes with 1 x SSC, 0.1% SDS; 0.5 x SSC, 0.1% SDS; 0.1 x SSC, 0.1% SDS at 68 °C for 15 minutes.

[0019] The nucleotide sequence SEQ. ID. No. 1 and SEQ. ID. No. 1099, respectively, has been obtained by sequenc-

ing the genome of and the plasmid contained in *Bifidobacterium longum* NCC2705 by the method of directed sequencing after fluorescent automated sequencing of the inserts of clones and assembling of these sequences of nucleotide fragments (inserts) by means of softwares. To this end, fragments of the genome were created, ligated into suitable vectors for amplification and propagation and the corresponding fragments were sequenced. Overlaps and the final arrangement of the fragments, the nucleotide sequence thereof, were assessed by the aid of appropriate softwares.

[0020] The present invention is further directed to nucleic acid molecules comprising open reading frames (ORFs) encoding *Bifidobacterium longum* proteins. Therefore, according to another aspect the present invention relates to a polynucleotide having a nucleotide sequence of an open reading frame (ORF) of a *Bifidobacterium longum* genome comprising, (a) a nucleotide sequence chosen from any one of Seq ID. No. 2 to SEQ. ID. NO. 1098; or (b) a nucleotide sequence exhibiting at least 95 %, preferably 96 %, 97 % 98 % and most preferably 99 % identity with any one of SEQ ID. NO. 2 to SEQ. ID. NO. 1098; or (c) a polynucleotide which hybridizes to any one of SEQ. ID. NO. 2 SEQ. ID. NO. 1098 under conditions of high stringency.

[0021] These nucleic acid molecules may be obtained, by e.g. specific amplification of the corresponding sequence using the polymerase chain reaction. Due to the sequence information provided herein the skilled person may design and synthesize any suitable primer nucleotide and amplify a fragment of interest using the polymerase chain reaction. Therefore, the present invention also comprises nucleotide sequences selected from sequence SEQ. ID. NO. 1 which can be used as a primer for the amplification of nucleic acid sequences. Other techniques for amplifying the target nucleic acid may of course be also be used, such as e.g. the TAS (Transcription-based Amplification System) technique, the 3SR (Self-Sustained Sequence Replication) technique, the NASBA (Nucleic Acid Sequence Based Amplification) technique, the SDA (Strand Displacement Amplification) technique or the TMA (Transcription Mediated Amplification) technique etc..

[0022] The (poly)nucleotides of the invention may also be used as probes and techniques for amplifying or modifying a nucleic acid serving as a probe, such as e.g. the LCR (Ligase Chain Reaction) technique, the RCR (Repair Chain Reaction) technique, the CPR (Cycling Probe Reaction) technique or the Q-beta-replicase amplification technique may well be applied.

[0023] The present invention, therefore, envisages both hybridization (detection) probes and primers for detecting a nucleotide sequence (target nucleotide) of the present invention. In the case of the target being a RNA molecule, e. g. a mRNA, said mRNA may be directly detected or transformed to a cDNA prior to detection.

[0024] Alternatively, in order to obtain fragments of the nucleic acid represented by SEQ. ID. NO.1 the *Bifidobacterium longum* genomic DNA may be subjected to digestion with selected restriction enzymes, with the fragments being separated by e.g. electrophoresis or another suitable separation technique. Such techniques are well known in the art and are inter alia disclosed in Sambrook et al. A Laboratory Manual, Cold Spring Harbor, 1992. Such fragments may easily be obtained by isolating the genomic DNA of *Bifidobacterium longum* NCC2705 (CNCM I-2618) and performing the necessary steps.

[0025] In an alternative form the nucleic acids may also be obtained by chemical synthesis when they are not too large in size according to methods well known to a person skilled in the art.

[0026] Modified nucleotide sequences shall be understood to mean any nucleotide sequence obtained by mutagenesis according to techniques well known to a skilled person and exhibiting modifications in relation to the normal sequences, for example mutations in the regulatory and/or promoter sequences for the expression of a polypeptide, in particular leading to a modification of the level of expression of the said polypeptide or to a modulation of the replicative cycle. Modified nucleotide sequence will also be understood to mean any nucleotide sequence encoding a modified polypeptide as defined below.

[0027] The subject of the present invention also includes *Bifidobacterium longum* nucleotide sequences characterized in that they are selected from a nucleotide sequence having an open reading frame as identified by SEQ. ID. NO. 2 to SEQ. ID. NO. 1098, shown in the table I below.

Table I

Seq. ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ. ID. No.2	ORF3	785	2455	hsp60 heat shock protein	TREMBLNEW:AF240579_1	0
SEQ. ID. No.3	ORF7	3674	4447	phosphate response regulator protein phoP	PIR:H70705	7,00E-71
SEQ. ID. No.4	ORF10	4622	6489	two-component sensor histidine kinase	PIR:A70706	7,00E-51
SEQ. ID. No.5	ORF13	6542	6928	cold shock protein	PIR:G70816	1,00E-25
SEQ. ID. No.6	ORF14	6940	8124	Unknown	PIR:B70780	1,00E-35
SEQ. ID. No.7	ORF23	9354	11960	ATP-binding proteinase	PIR:T36384	0
SEQ. ID. No.8	ORF24	13462	12146	cytosine deaminase	TREMBLNEW:AE004481_2	9,00E-95
SEQ. ID. No.9	ORF28	15297	16670	membrane transport protein	TREMBLNEW:SC2G58_25	6,00E-88
SEQ. ID. No.10	ORF29	16759	17514	Creatinase	PIR:T44251	2,00E-60
SEQ. ID. No.11	ORF31	17689	19479	5'-nucleotidase	PIR:F75511	4,00E-20
SEQ. ID. No.12	ORF36	21148	19691	Unknown	PIR:B70506	2,00E-44
SEQ. ID. No.13	ORF38	21248	22845	histidyl-tRNA synthetase	PIRNEW:A82588	4,00E-68
SEQ. ID. No.14	ORF42	22594	24480	Aspartate-tRNA ligase	PIR:C70724	0
SEQ. ID. No.15	ORF47	26476	27288	glutamate uptake system ATP-binding protein	PIR:T35147	1,00E-102
SEQ. ID. No.16	ORF48	27362	28159	glutamate-binding periplasmic protein	PIR:T35146	5,00E-72
SEQ. ID. No.17	ORF49	28162	28836	glutamate transport protein gluC	PIR:T35145	2,00E-47
SEQ. ID. No.18	ORF50	28845	29942	glutamate transport protein gluD	PIR:T35144	5,00E-40
SEQ. ID. No.19	ORF51	30034	31572	acid phosphatase	PIR:T28698	3,00E-50
SEQ. ID. No.20	ORF57	32653	33576	Unknown	PIR:D75557	6,00E-46
SEQ. ID. No.21	ORF60	33713	36277	helicase-like protein	PIR:T17732	5,00E-42
SEQ. ID. No.22	ORF64	36363	37739	ATP/GTP binding protein	TREMBLNEW:SC9C5_30	1,00E-119
SEQ. ID. No.23	ORF65	37800	38519	sensory response regulator	PIR:H70592	5,00E-49
SEQ. ID. No.24	ORF67	38519	40213	two-component sensory histidine kinase	PIR:G70592	1,00E-68
SEQ. ID. No.25	ORF74	42259	43239	Periplasmic sugar-binding protein	PIR:S56453	2,00E-31

Table I (continued)

Seq. ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ. ID. No. 26	ORF75	43383	44921	nbose ABC transporter, ATP-binding protein	PIRNEW:A82497	1,00E-100
SEQ. ID. No. 27	ORF76	44926	45993	carbohydrate transport protein	PIR:S56456	2,00E-44
SEQ. ID. No. 28	ORF78	45993	47012	high affinity sugar transport protein rbsC	PIR:S56457	4,00E-30
SEQ. ID. No. 29	ORF79	48695	47241	Permease	TREMBL:OOE250422_3	1,00E-54
SEQ. ID. No. 30	ORF83	49084	49977	2-hydroxyacid dehydrogenase family	PIRNEW:T50667	2,00E-30
SEQ. ID. No. 31	ORF90	54950	52521	methyl coenzyme M reductase system, component A2	PIR:D69159	7,00E-56
SEQ. ID. No. 32	ORF99	58071	58835	polyphosphate glucokinase	PIR:E75472	4,00E-53
SEQ. ID. No. 33	ORF101	59063	60319	aminotransferase	PIR:T37220	4,00E-22
SEQ. ID. No. 34	ORF103	60331	61152	ABC transporter, ATP-binding protein	PIR:B75270	3,00E-23
SEQ. ID. No. 35	ORF113	67189	69948	DNA ligase	PIR:T35810	1,00E-131
SEQ. ID. No. 36	ORF114	70127	71239	Unknown (ATP-binding protein)	TREMBLNEW:SCP8_15	2,00E-79
SEQ. ID. No. 37	ORF119	72964	73776	sugar transport protein	TREMBL:SCE59_3	1,00E-45
SEQ. ID. No. 38	ORF129	77028	77984	3-hydroxyacyl-CoA dehydrogenase	PIR:A69252	2,00E-41
SEQ. ID. No. 39	ORF131	78166	79272	Unknown	TREMBL:SCF41_25	3,00E-43
SEQ. ID. No. 40	ORF137	80448	81182	Unknown	PIR:A69760	3,00E-25
SEQ. ID. No. 41	ORF139	82012	81215	Unknown	PIR:S76205	2,00E-36
SEQ. ID. No. 42	ORF141	82797	82012	ABC-type transport system ATP-binding protein	PIRNEW:F82198	5,00E-20
SEQ. ID. No. 43	ORF145	82902	83465	translation-elongation factor	PIR:B70658	4,00E-67
SEQ. ID. No. 44	ORF146	83523	84092	transcription termination protein	PIR:A70658	5,00E-21
SEQ. ID. No. 45	ORF147	83803	85506	carbamoyl-phosphate synthetase	PIR:D70959	1,00E-120
SEQ. ID. No. 46	ORF148	85511	88891	Carbamoyl-phosphate synthase large chain	PIR:A70980	0
SEQ. ID. No. 47	ORF149	88894	89811	orotidine-5'-phosphate decarboxylase	PIR:B49930	6,00E-40
SEQ. ID. No. 48	ORF151	89994	90581	guanylate kinase	PIR:C70899	6,00E-44
SEQ. ID. No. 49	ORF152	91293	90589	DNA polymerase III	PIR:C72360	4,00E-22
SEQ. ID. No. 50	ORF156	91440	93692	translation elongation factor EF-G homolog	TREMBL:BF7ETAQ3_2	3,00E-64

Table I (continued)

Seq. ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ. ID. No. 51	ORF160	94496	95239	amino acid ABC transporter, permease protein	PIR:D71849	4,00E-53
SEQ. ID. No. 52	ORF162	95229	95900	amino-acid ABC transporter integral membrane protein	PIR:G81391	5,00E-49
SEQ. ID. No. 53	ORF165	95896	96684	amino acid ABC transporter, ATP-binding protein	PIR:F71849	7,00E-64
SEQ. ID. No. 54	ORF166	96753	97652	amino acid binding protein	TREMBL:U60994_4	1,00E-72
SEQ. ID. No. 55	ORF168	97891	99126	cystathionine beta-lyase	PIRNEW:T47232	8,00E-95
SEQ. ID. No. 56	ORF170	101042	99774	transposase	TREMBL:REU10061_1	4,00E-78
SEQ. ID. No. 57	ORF176	102563	103459	Unknown	TREMBL:AC008261_3	2,00E-46
SEQ. ID. No. 58	ORF180	105297	104506	glutamate racemase	PIR:C69978	3,00E-39
SEQ. ID. No. 59	ORF182	105456	106295	Diaminopimelate epimerase	PIR:T35113	5,00E-30
SEQ. ID. No. 60	ORF186	107179	108069	Unknown	TREMBLNEW:SCP8_24	8,00E-37
SEQ. ID. No. 61	ORF191	110307	111878	ATP-dependent DNA helicase	TREMBLNEW:SC23B6_12	3,00E-82
SEQ. ID. No. 62	ORF194	113698	111954	Unknown	TREMBLNEW:SC23B6_23	5,00E-35
SEQ. ID. No. 63	ORF197	113917	114795	Unknown	PIR:T36157	1,00E-42
SEQ. ID. No. 64	ORF199	114914	115327	Unknown	PIR:T44716	1,00E-24
SEQ. ID. No. 65	ORF202	117499	118686	1-deoxy-D-xylulose 5-phosphate reductoisomerase	PIR:A70923	1,00E-103
SEQ. ID. No. 66	ORF203	118698	119906	peptidoglycan acetylation	PIR:T35407	1,00E-135
SEQ. ID. No. 67	ORF205	121792	122508	Unknown	TREMBL:SCC121_13	7,00E-47
SEQ. ID. No. 68	ORF206	122454	123299	undecaprenyl phosphate synthetase	PIR:H70585	5,00E-77
SEQ. ID. No. 69	ORF211	125854	124787	Unknown	PIR:C72369	1,00E-25
SEQ. ID. No. 70	ORF212	126895	126116	ABC transporter, permease protein	PIR:D72369	6,00E-26
SEQ. ID. No. 71	ORF214	128647	127094	sucrose hydrolase	PIR:S52162	3,00E-91
SEQ. ID. No. 72	ORF216	130160	128661	sucrose transport protein	PIR:GRECST	1,00E-92
SEQ. ID. No. 73	ORF217	131250	130213	transcription regulator, LacI family	PIR:F72282	3,00E-31
SEQ. ID. No. 74	ORF219	132691	131297	Serpin	SWISSPROT:NEUS_MOUSE	5,00E-30
SEQ. ID. No. 75	ORF225	135167	133791	membrane transport protein	PIR:G64937	3,00E-48

Table I (continued)

Seq. ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ. ID. No.76	ORF229	137121	136123	phosphomethylpyrimidine kinase	PIR:T35647	3,00E-48
SEQ. ID. No.77	ORF232	140189	137439	thiamin biosynthesis protein thIA	PIR:D69722	0
SEQ. ID. No.78	ORF235	141216	140275	hydroxyethylthiazole kinase	TREMBLNEW:AP001297_22	1,00E-28
SEQ. ID. No.79	ORF238	141652	143121	glycyl-tRNA synthetase	PIR:D70585	0
SEQ. ID. No.80	ORF239	143269	144510	transcription regulator	TREMBL:SCC82_3	1,00E-100
SEQ. ID. No.81	ORF240	144625	145833	ftsZ protein	PIR:JE0282	1,00E-92
SEQ. ID. No.82	ORF246	148841	149800	ribosomal large subunit pseudouridine synthase	PIR:T34943	1,00E-67
SEQ. ID. No.83	ORF254	152161	155727	DNA-directed DNA polymerase III alpha chain	PIR:T35093	0
SEQ. ID. No.84	ORF257	156459	158333	protoporphyrinogen oxidase	TREMBL:SP09352_2	1,00E-175
SEQ. ID. No.85	ORF290	172284	171292	transposase	PIR:T14971	5,00E-33
SEQ. ID. No.86	ORF292	173573	172074	transposase	TREMBLNEW:AP001520_222	4,00E-52
SEQ. ID. No.87	ORF297	176631	174295	phage infection protein	PIR:E69115	6,00E-65
SEQ. ID. No.88	ORF299	179366	176631	phage infection protein	PIR:E69115	1,00E-65
SEQ. ID. No.89	ORF303	180792	179875	NADPH-flavin oxidoreductase	PIR:S39698	1,00E-21
SEQ. ID. No.90	ORF305	181144	181788	Unknown	TREMBL:SC9G1_8	3,00E-24
SEQ. ID. No.91	ORF307	182199	183524	Sugar-binding protein	TREMBL:CTPULSA_3	2,00E-35
SEQ. ID. No.92	ORF310	184801	183788	Transcriptional regulators of the LacI family	TREMBL:SCF43_17	2,00E-30
SEQ. ID. No.93	ORF311	185082	186035	sugar transport system permease	PIR:S37704	2,00E-47
SEQ. ID. No.94	ORF313	186038	186877	ABC transporter sugar permease	PIR:S37705	3,00E-50
SEQ. ID. No.95	ORF318	187883	190756	arabinosidase	TREMBL:BF55187_1	4,00E-41
SEQ. ID. No.96	ORF323	192387	191209	transposase	TREMBLNEW:TFU66426_1	1,00E-64
SEQ. ID. No.97	ORF327	192648	194147	transposase	TREMBLNEW:AP001520_222	3,00E-53
SEQ. ID. No.98	ORF330	193937	194929	probable transposase	PIR:T14971	5,00E-33
SEQ. ID. No.99	ORF333	195262	196671	Unknown	PIR:C71089	4,00E-76
SEQ. ID. No.100	ORF334	198212	196740	aromatic amino acid transport protein	PIR:QRECA	4,00E-96

Table I (continued)

Seq. ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ. ID. No. 101	ORF335	199003	198437	transcriptional regulator (TetR/AcrR family)	TREMBLNEW:AP001509_157	2,00E-23
SEQ. ID. No. 102	ORF337	199147	199845	ABC transporter, ATP-binding protein	PIR:B69477	7,00E-61
SEQ. ID. No. 103	ORF345	203871	205394	amino acid permease	PIR:B69580	2,00E-82
SEQ. ID. No. 104	ORF348	205839	210554	Unknown	TREMBL:SC6D11_2	3,00E-88
SEQ. ID. No. 105	ORF351	210769	214602	Unknown	TREMBLNEW:AB013390_9	5,00E-38
SEQ. ID. No. 106	ORF358	215664	215104	DNA-damage-inducible protein	SWISSPROT:DIND_ECOLI	1,00E-24
SEQ. ID. No. 107	ORF363	216808	218676	ABC transporter (ATP-binding protein)	TREMBL:SC7A8_2	1,00E-115
SEQ. ID. No. 108	ORF365	218894	220720	ABC transporter	TREMBL:SC7A8_3	1,00E-136
SEQ. ID. No. 109	ORF372	223915	225009	Unknown	TREMBL:SCE87_4	2,00E-63
SEQ. ID. No. 110	ORF377	226371	228233	methionine-tRNA ligase	PIR:D71091	1,00E-113
SEQ. ID. No. 111	ORF382	232054	230531	aminopeptidase	TREMBL:LNHEPC_1	4,00E-47
SEQ. ID. No. 112	ORF384	232279	234504	Unknown	PIR:F72395	1,00E-98
SEQ. ID. No. 113	ORF389	236829	235675	lacI-family transcriptional regulator	TREMBLNEW:SCG22_12	4,00E-34
SEQ. ID. No. 114	ORF393	237203	238609	alpha galactosidase	TREMBLNEW:AP001513_143	1,00E-95
SEQ. ID. No. 115	ORF396	239413	241272	ABC transporter	TREMBLNEW:AP001511_14	1,00E-105
SEQ. ID. No. 116	ORF397	241286	243091	ABC transporter (ATP-binding protein)	PIR:S72638	1,00E-142
SEQ. ID. No. 117	ORF399	243351	245819	alpha-L-arabinofuranosidase I	PIR:T36818	1,00E-108
SEQ. ID. No. 118	ORF404	247917	246175	arabinan endo-1,5-alpha-L-arabinosidase homolog	PIR:E70076	3,00E-44
SEQ. ID. No. 119	ORF406	249669	248077	arabinan endo-1,5-alpha-L-arabinosidase	PIR:E70076	4,00E-60
SEQ. ID. No. 120	ORF413	252032	253087	transcription regulator, LacI family	TREMBLNEW:SCG22_12	6,00E-66
SEQ. ID. No. 121	ORF419	254388	255443	alpha-L-arabinofuranosidase II	TREMBLNEW:AP001513_140	1,00E-108
SEQ. ID. No. 122	ORF424	257319	258269	ABC transporter sugar permease	PIRNEW:D82557	1,00045
SEQ. ID. No. 123	ORF427	258269	259192	membrane transport protein	PIR:A56641	1,00048
SEQ. ID. No. 124	ORF433	261148	262104	Unknown	TREMBL:SCE87_2	2,00E-57
SEQ. ID. No. 125	ORF436	262540	264747	potassium uptake protein	PIRNEW:F82623	4,00E-78

Table I (continued)

Seq. ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ. ID. No. 126	ORF456	274558	276960	Unknown	PIR:T00092	2,00E-67
SEQ. ID. No. 127	ORF463	279189	278236	glycosyltransferase homolog	TREMBL:AF033015_6	4,00E-75
SEQ. ID. No. 128	ORF465	282221	280941	polysaccharide ABC transporter	PIR:T00089	1,00E-102
SEQ. ID. No. 129	ORF466	283047	282226	ABC-type transport protein	PIR:T00088	2,00E-59
SEQ. ID. No. 130	ORF469	284425	284814	glycerol-3-phosphate cytidyltransferase	PIR:A49757	1,00E-44
SEQ. ID. No. 131	ORF472	288030	286135	Unknown	PIR:D70888	4,00E-21
SEQ. ID. No. 132	ORF475	288829	289782	Glycosyltransferase-type protein	TREMBL:AF033015_6	6,00E-76
SEQ. ID. No. 133	ORF476	289796	291790	transferase	PIR:D70888	2,00E-95
SEQ. ID. No. 134	ORF477	293831	291894	Unknown	PIR:D70888	4,00E-95
SEQ. ID. No. 135	ORF479	294815	294189	Unknown	PIR:T00092	3,00E-22
SEQ. ID. No. 136	ORF482	294973	295959	transposase	TREMBL:NEW.TFU66426_1	7,00E-69
SEQ. ID. No. 137	ORF484	296743	295985	probable transposase	PIR:T14971	7,00E-37
SEQ. ID. No. 138	ORF489	298223	297207	transposase	TREMBL:NEW.AP001520_222	5,00E-57
SEQ. ID. No. 139	ORF496	300685	300095	transposase	TREMBL:AF029727_1	1,00E-28
SEQ. ID. No. 140	ORF503	304082	303180	glucose-1-phosphate thymidyltransferase	TREMBL:AB030032_7	1,00E-108
SEQ. ID. No. 141	ORF504	305615	304176	dTDP-4-keto-6-deoxyglucose-3,5-epimerase	TREMBL:SMD182_5	9,00E-58
SEQ. ID. No. 142	ORF506	306672	305632	dTDP-glucose-4,6-dehydratase	TREMBL:AF105113_5	1,00E-124
SEQ. ID. No. 143	ORF508	308254	306818	polysaccharide biosynthesis (cps-like)	TREMBL:A76918_12	2,00E-58
SEQ. ID. No. 144	ORF509	310121	308379	2-succinyl-6-hydroxy-24-cyclohexadiene-1-carboxylate synthase	PIR:G69656	5,00E-24
SEQ. ID. No. 145	ORF510	310888	310151	dehydrogenase-like	PIR:S39737	3,00E-25
SEQ. ID. No. 146	ORF514	314448	313510	glycosyltransferase	TREMBL:AF028471_9	1,00E-105
SEQ. ID. No. 147	ORF515	315657	314467	putative rhamnosyl transferase	TREMBL:AF028471_8	1,00E-138
SEQ. ID. No. 148	ORF516	317259	315718	glycosyl transferase	TREMBL:SCF62_7	6,00E-47
SEQ. ID. No. 149	ORF529	321876	321079	transposase	PIR:B60340	5,00E-25

Table 1 (continued)

Seq. ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ. ID. No. 150	ORF542	326223	325735	transposase	PIR:B60340	7,00E-24
SEQ. ID. No. 151	ORF546	327618	329354	Undecaprenyl-phosphate glucose 1-phosphate transferase	TREMBL:SCF62_7	4,00E-59
SEQ. ID. No. 152	ORF553	331662	333176	multidrug resistance protein	PIR:F69763	2,00E-73
SEQ. ID. No. 153	ORF554	334646	333282	transmembrane protein	TREMBL:MBO5699_1	1,00E-100
SEQ. ID. No. 154	ORF557	336993	336313	Unknown	PIR:A70672	7,00E-34
SEQ. ID. No. 155	ORF558	337926	337060	oxidoreductase	PIR:T34993	4,00E-68
SEQ. ID. No. 156	ORF561	341255	338565	arabinogalactanendo-1,4-beta-galactosidase	TREMBL:NEW:AP001514_29	1,00E-141
SEQ. ID. No. 157	ORF563	342506	341454	transcription regulator, LacI family	PIR:F72282	2,00E-28
SEQ. ID. No. 158	ORF564	344823	342553	beta-galactosidase	TREMBL:SC6D11_3	1,00E-164
SEQ. ID. No. 159	ORF566	345876	344872	ABC transporter sugar permease	TREMBL:SC6D11_5	1,00E-113
SEQ. ID. No. 160	ORF567	346841	345882	ABC transporter sugar permease	TREMBL:SC6D11_6	6,00E-80
SEQ. ID. No. 161	ORF570	348409	347063	solute-binding lipoprotein	TREMBL:SC6D11_4	3,00E-88
SEQ. ID. No. 162	ORF574	353922	349792	ABC transporter	TREMBL:HI32749_4	6,00E-95
SEQ. ID. No. 163	ORF578	354795	356615	long chain fatty acid coA ligase	PIR:T35513	1,00E-127
SEQ. ID. No. 164	ORF581	357435	356803	ABC transporter, ATP-binding protein	TREMBL:AF140784_2	6,00E-61
SEQ. ID. No. 165	ORF582	358671	357451	vex(vexp1) homolog	TREMBL:AF140784_1	2,00E-30
SEQ. ID. No. 166	ORF585	360038	358671	ABC transporter	TREMBL:AF140784_3	3,00E-56
SEQ. ID. No. 167	ORF591	362034	362747	Unknown	PIR:T36850	4,00E-26
SEQ. ID. No. 168	ORF593	364451	362937	L-arabinose isomerase	TREMBL:AB036736_2	1,00E-135
SEQ. ID. No. 169	ORF594	365375	364686	L-ribose-phosphate 4-epimerase	TREMBL:AB036736_1	1,00E-47
SEQ. ID. No. 170	ORF597	367106	365463	xylulose kinase	TREMBL:PSP249910_1	2,00E-22
SEQ. ID. No. 171	ORF598	368415	367264	Transcriptional regulators of the LacI family	TREMBL:SC6D11_7	1,00E-39
SEQ. ID. No. 172	ORF600	369342	368506	ribonuclease HII	PIR:T35186	4,00E-26
SEQ. ID. No. 173	ORF603	370319	369465	signal peptidase I	TREMBL:SLTK24SIP_1	2,00E-33
SEQ. ID. No. 174	ORF606	373183	371486	Gglucose-6-phosphate isomerase	PIR:H70715	0

Table I (continued)

Seq.ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ. ID. No.175	ORF611	376269	374992	Antibiotic resistance factor	TREMBL:NEW.SPN277485_1	1,00E-47
SEQ. ID. No.176	ORF613	377629	376322	peptidoglycan biosynthesis	TREMBL:SSU66883_4	2,00E-38
SEQ. ID. No.177	ORF615	379262	377706	beta-lactam resistance factor	TREMBL:NEW.SPN277485_1	3,00E-59
SEQ. ID. No.178	ORF620	380176	379421	Unknown	PIR:T36125	2,00E-46
SEQ. ID. No.179	ORF621	380996	380223	ribonuclease PH	PIR:T36127	6,00E-82
SEQ. ID. No.180	ORF623	382637	381282	Unknown	PIR:T36140	1,00E-124
SEQ. ID. No.181	ORF627	384144	385151	Ion Channel	TREMBL:ILLU60828_1	1,00E-105
SEQ. ID. No.182	ORF634	387400	387876	Unknown	PIR:T35654	4,00E-23
SEQ. ID. No.183	ORF636	388205	389035	ribonuclease	PIR:T44706	2,00E-44
SEQ. ID. No.184	ORF638	389199	391163	Acetolactate synthase	PIR:T35828	0
SEQ. ID. No.185	ORF639	391183	391734	acetolactate synthase	PIR:JC7166	5,00E-52
SEQ. ID. No.186	ORF643	394929	392656	ABC transporter	PIR:G70817	9,00E-91
SEQ. ID. No.187	ORF644	395867	394980	amino transferase	PIR:S75988	2,00E-21
SEQ. ID. No.188	ORF645	395810	397561	cysteine-tRNA ligase	PIR:B70607	1,00E-110
SEQ. ID. No.189	ORF647	398700	400445	signal recognition particle protein (fih)	PIR:T34771	1,00E-159
SEQ. ID. No.190	ORF650	401867	402325	30S ribosomal protein S16	PIR:H70927	2,00E-22
SEQ. ID. No.191	ORF652	402605	403225	Unknown	PIR:T34778	3,00E-20
SEQ. ID. No.192	ORF653	404403	403354	inosine-uridine preferring nucleoside hydrolase	PIR:B75524	2,00E-40
SEQ. ID. No.193	ORF655	405364	404504	oxidoreductase	PIR:B75341	2,00E-32
SEQ. ID. No.194	ORF661	408342	407767	Unknown	TREMBL:LMU66186_1	1,00E-38
SEQ. ID. No.195	ORF663	409416	408640	phosphate ABC transporter	PIR:D70810	6,00E-98
SEQ. ID. No.196	ORF664	410434	409472	phosphate transport system permease protein A-1	PIR:B70584	3,00E-49
SEQ. ID. No.197	ORF666	411420	410470	phosphate transport system permease protein	TREMBL:NEW.SCD84_8	4,00E-56
SEQ. ID. No.198	ORF669	412764	411634	Phosphate-binding protein	TREMBL:ML15182_25	3,00E-41
SEQ. ID. No.199	ORF671	413774	413007	two-component response regulator	TREMBL:MBY13627_3	3,00E-75

Table I (continued)

Seq.ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ.ID. No.200	ORF672	415238	413910	two-component sensor histidine kinase	PIR:E70744	9,00E-44
SEQ.ID. No.201	ORF676	417556	416327	2-dehydro-3-deoxyphosphoheptonate aldolase	PIR:140837	1,00E-92
SEQ.ID. No.202	ORF677	418818	417688	2-dehydro-3-deoxyphosphoheptonate aldolase	PIR:ADECHF	2,00E-96
SEQ.ID. No.203	ORF678	420453	419113	cysteine aminopeptidase	PIR:S52865	3,00E-88
SEQ.ID. No.204	ORF679	422145	420571	Unknown	TREMBL:SC8F4_	1,00E-21
SEQ.ID. No.205	ORF681	422970	422296	pyroglutaryl-peptidase I	PIR:S23432	4,00E-26
SEQ.ID. No.206	ORF683	423855	422983	CDP-ribitol pyrophosphorylase	PIR:S60902	9,00E-32
SEQ.ID. No.207	ORF684	424915	423938	Unknown	PIR:T34951	2,00E-33
SEQ.ID. No.208	ORF686	426819	424986	protease	TREMBLNEW:AP001511_163	2,00E-66
SEQ.ID. No.209	ORF689	426773	427525	tRNA (guanine-N1)-methyltransferase	PIR:E70927	8,00E-53
SEQ.ID. No.210	ORF690	428172	427555	methylase	PIR:C70671	1,00E-26
SEQ.ID. No.211	ORF691	431233	428393	ATP-dependent DNA helicase	PIR:T35650	1,00E-108
SEQ.ID. No.212	ORF696	433135	434409	Unknown	PIR:B70078	7,00E-86
SEQ.ID. No.213	ORF704	435955	436485	methylated-DNA-protein-cysteine methyltransferase	PIR:T34664	9,00E-21
SEQ.ID. No.214	ORF709	439060	440586	L-asparagine	TREMBL:AF181498_4	1,00E-124
SEQ.ID. No.215	ORF713	444121	442847	polyamine ABC-transporter ATP-binding protein	PIR:T35802	2,00E-52
SEQ.ID. No.216	ORF718	446161	444980	ABC transport system permease	PIR:E81344	2,00E-27
SEQ.ID. No.217	ORF720	447105	445942	Unknown	TREMBLNEW:AE004747_11	4,00E-29
SEQ.ID. No.218	ORF721	448644	447361	D-alanine:D-alanine ligase	PIR:B70673	6,00E-75
SEQ.ID. No.219	ORF723	449733	448735	glycerol-3-phosphate dehydrogenase	PIR:T35643	4,00E-79
SEQ.ID. No.220	ORF737	455903	456889	peptidylprolyl isomerase	TREMBL:SC141_22	2,00E-25
SEQ.ID. No.221	ORF740	457747	456941	Unknown	PIR:E70769	1,00E-60
SEQ.ID. No.222	ORF742	459561	458092	H+-transporting ATP synthase beta chain	PIR:S37547	0
SEQ.ID. No.223	ORF744	460493	459573	ATP synthase gamma subunit	TREMBLNEW:SC26G5_16	1,00E-62
SEQ.ID. No.224	ORF747	462128	460500	H+-transporting ATP synthase	TREMBLNEW:SC26G5_15	0

Table I (continued)

Seq.ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ.ID. No.225	ORF748	463040	462207	ATP synthase delta chain	TREMBLNEW:SC26G5_14	4,00E-24
SEQ.ID. No.226	ORF751	464793	463984	H ⁺ -transporting ATP synthase	PIR:S37541	1,00E-21
SEQ.ID. No.227	ORF755	466289	465258	homoserine O-succinyltransferase	TREMBLNEW:AP001515_14	2,00E-88
SEQ.ID. No.228	ORF774	472562	473587	Bacteriophage portal protein	TREMBL:BPH6589_4	1,00E-22
SEQ.ID. No.229	ORF780	477113	479179	Unknown	TREMBL:LLHORF02_9	2,00E-27
SEQ.ID. No.230	ORF793	483906	483079	Integrase	PIR:B70965	2,00E-47
SEQ.ID. No.231	ORF802	486594	488831	alpha-amylase	TREMBL:SC6A11_19	1,00E-174
SEQ.ID. No.232	ORF807	489062	489553	inorganic pyrophosphatase	PIR:T36335	2,00E-48
SEQ.ID. No.233	ORF809	489790	490371	Unknown	PIR:F81434	6,00E-27
SEQ.ID. No.234	ORF812	491348	492145	two-component response regulator	PIR:JN0831	5,00E-66
SEQ.ID. No.235	ORF817	492207	492890	Endonuclease III	PIR:C70790	6,00E-58
SEQ.ID. No.236	ORF821	494520	497357	valine-tRNA ligase	PIR:B71675	1,00E-149
SEQ.ID. No.237	ORF828	502513	500447	transcription termination factor Rho	TREMBL:MLRHO_1	1,00E-151
SEQ.ID. No.238	ORF832	504332	502722	Unknown	PIR:B71153	1,00E-29
SEQ.ID. No.239	ORF840	509762	508266	Glu-tRNA(Gln) amidotransferase chain B	PIR:T35817	1,00E-170
SEQ.ID. No.240	ORF842	511329	509791	Glu-tRNA(Gln) amidotransferase chain A	PIR:T35815	1,00E-158
SEQ.ID. No.241	ORF845	512647	511802	Unknown	PIR:G70833	6,00E-35
SEQ.ID. No.242	ORF848	514770	513370	Unknown	TREMBL:AF213822_7	7,00E-55
SEQ.ID. No.243	ORF850	515115	514837	Unknown	PIR:A70907	1,00E-28
SEQ.ID. No.244	ORF852	515227	517932	copper-transporting ATPase	TREMBL:AF129004_1	1,00E-113
SEQ.ID. No.245	ORF853	518753	518022	glycerol uptake facilitator protein	PIR:B72254	3,00E-47
SEQ.ID. No.246	ORF855	520666	518990	phosphotransferase system enzyme I	TREMBLNEW:AP001517_195	1,00E-129
SEQ.ID. No.247	ORF857	521759	521316	ribosomal protein L9	PIR:T36596	2,00E-25
SEQ.ID. No.248	ORF859	522744	522091	single-strand binding protein	PIR:F70913	6,00E-39
SEQ.ID. No.249	ORF861	523094	522804	ribosomal protein S6	PIR:E70913	1,00E-21

Table I (continued)

Seq. ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ. ID. No.250	ORF884	523860	524870	ribose-phosphate pyrophosphokinase	TREMBLNEW:SCE66_2	1,00E-104
SEQ. ID. No.251	ORF885	525833	524952	Unknown	PIRNEW:H82646	6,00E-29
SEQ. ID. No.252	ORF888	529629	525916	endo-1,4-beta-xylanase	PIR:H69735	1,00E-24
SEQ. ID. No.253	ORF873	535559	529737	Unknown	PIR:T17479	0
SEQ. ID. No.254	ORF881	538453	536261	Unknown	PIR:F72395	1,00E-101
SEQ. ID. No.255	ORF885	539055	538240	Sugar permeases	PIR:T30595	1,00E-38
SEQ. ID. No.256	ORF887	540002	539079	sugar transport system permease	PIR:T36087	7,00E-30
SEQ. ID. No.257	ORF892	542101	543120	Transcriptional regulators of the LacI family	TREMBL:AF086819_1	3,00E-40
SEQ. ID. No.258	ORF893	544958	543141	ABC-type transport protein	PIR:S38903	4,00E-79
SEQ. ID. No.259	ORF897	546143	545394	cobyrinic acid synthase	PIR:T31439	2,00E-47
SEQ. ID. No.260	ORF899	547718	546249	UDP-N-acetylmuramyl tripeptide synthetase	PIR:T31440	7,00E-28
SEQ. ID. No.261	ORF904	549247	547721	replicative DNA helicase	PIR:T36598	1,00E-144
SEQ. ID. No.262	ORF905	549303	550895	DNA-damage-inducible protein f	PIR:T36597	5,00E-69
SEQ. ID. No.263	ORF908	552758	550935	protein pil uridylyltransferase	PIR:T34770	3,00E-83
SEQ. ID. No.264	ORF911	554501	553209	ammonium transport protein	TREMBL:CAJ10319_2	2,00E-90
SEQ. ID. No.265	ORF914	556131	554872	prokaryotic docking protein	PIR:T35664	1,00E-88
SEQ. ID. No.266	ORF915	556236	557072	transcription regulator	TREMBLNEW:SCE66_8	1,00E-56
SEQ. ID. No.267	ORF917	557099	558130	glycosyl transferase	TREMBL:SPAJ6986_9	2,00E-30
SEQ. ID. No.268	ORF918	559943	558210	dipeptidase	TREMBL:LDIPEP_1	2,00E-90
SEQ. ID. No.269	ORF921	560036	561700	Glucose-6-phosphate 1-dehydrogenase	PIR:T36009	0
SEQ. ID. No.270	ORF922	561700	562722	Unknown	PIR:T35159	1,00E-57
SEQ. ID. No.271	ORF925	562862	563791	glucose-6-phosphate 1-dehydrogenase	PIR:T36011	9,00E-35
SEQ. ID. No.272	ORF927	565552	564101	6-phosphogluconate dehydrogenase	PIR:D70664	1,00E-167
SEQ. ID. No.273	ORF931	567372	569999	PHAGE INFECTION PROTEIN	SWISSPROT:PIP_LACLA	3,00E-35
SEQ. ID. No.274	ORF934	569999	572158	phage infection protein	PIR:E69115	2,00E-59

Table I (continued)

Seq. ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ. ID. No. 275	ORF941	574357	573563	ABC transport system ATP-binding protein	PIR:D81263	2,00E-65
SEQ. ID. No. 276	ORF945	576934	575633	ABC transport system permease protein	PIR:T47014	2,00E-61
SEQ. ID. No. 277	ORF949	579066	578386	Unknown	PIR:A40182	9,00E-36
SEQ. ID. No. 278	ORF951	581052	579244	Unknown	PIR:B71257	2,00E-39
SEQ. ID. No. 279	ORF956	582828	582190	Unknown	PIR:E70063	4,00E-32
SEQ. ID. No. 280	ORF959	582996	583352	Unknown	PIR:D81250	5,00E-29
SEQ. ID. No. 281	ORF965	586420	585539	Transposase	TREMBL:ECIS1397_2	6,00E-46
SEQ. ID. No. 282	ORF972	593430	587533	Unknown	PIR:T29435	1,00E-142
SEQ. ID. No. 283	ORF975	593599	594780	transposase	TREMBL:NEW:AB032203_2	1,00E-48
SEQ. ID. No. 284	ORF983	598200	596883	glutamyl-tRNA synthase	PIR:T45422	1,00E-163
SEQ. ID. No. 285	ORF987	600974	600060	Unknown	PIR:NEW:G82131	8,00E-25
SEQ. ID. No. 286	ORF991	602769	602113	Unknown	PIR:H70544	7,00E-31
SEQ. ID. No. 287	ORF994	603031	604473	Unknown	PIR:T35894	2,00E-25
SEQ. ID. No. 288	ORF998	607523	606009	formate tetrahydrofolate ligase	PIR:NEW:E81981	5,00E-41
SEQ. ID. No. 289	ORF1000	609284	607686	dipeptidase	TREMBL:LDIPEP_1	1,00E-105
SEQ. ID. No. 290	ORF1004	610300	611799	transposase	TREMBL:NEW:AP001520_222	4,00E-52
SEQ. ID. No. 291	ORF1007	611589	612581	probable transposase	PIR:T14971	5,00E-33
SEQ. ID. No. 292	ORF1010	613847	612690	DNA polymerase	PIR:T36661	6,00E-57
SEQ. ID. No. 293	ORF1013	614425	613847	thymidylate kinase	PIR:T36663	8,00E-47
SEQ. ID. No. 294	ORF1015	617834	614745	DNA topoisomerase I	PIR:T36664	0
SEQ. ID. No. 295	ORF1022	619472	621883	penicillin-binding protein	PIR:T36588	2,00E-72
SEQ. ID. No. 296	ORF1026	623874	621961	Alpha-isopropyl maleate synthase	PIR:G70794	0
SEQ. ID. No. 297	ORF1032	626934	628025	aspartate-semialdehyde dehydrogenase	PIR:A44846	3,00E-71
SEQ. ID. No. 298	ORF1034	628652	628113	aspartokinase	PIR:T35383	3,00E-39
SEQ. ID. No. 299	ORF1035	629496	628735	aspartate kinase alpha chain	PIR:S42422	2,00E-86

Table I (continued)

Seq.ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ.ID. No.300	ORF1037	631140	629860	Unknown	TREMBL:AF179376_1	4,00E-67
SEQ.ID. No.301	ORF1040	632029	633159	fimbria-associated protein	TREMBL:AF019629_2	5,00E-41
SEQ.ID. No.302	ORF1041	633761	633162	recombination protein	PIR:T35386	3,00E-70
SEQ.ID. No.303	ORF1042	636699	633790	DNA polymerase III subunit	TREMBL:SCD25_3	1,00E-115
SEQ.ID. No.304	ORF1045	638822	637695	Unknown	PIR:H70861	3,00E-21
SEQ.ID. No.305	ORF1052	642575	641511	secretory protein	PIR:T36677	1,00E-41
SEQ.ID. No.306	ORF1056	644480	643758	Unknown function (dedA like protein)	PIR:XMECAD	1,00E-29
SEQ.ID. No.307	ORF1059	646218	645418	3-oxoacyl-[acyl-carrier-protein] reductase	TREMBL:NEW.AP001515_225	2,00E-41
SEQ.ID. No.308	ORF1064	650268	648919	xanthine permease	PIR:C75614	1,00E-44
SEQ.ID. No.309	ORF1067	651128	650544	heat shock transcription regulator	PIR:S70209	6,00E-20
SEQ.ID. No.310	ORF1068	652162	651146	heat shock chaperone protein DNAJ-like	PIR:S76622	2,00E-26
SEQ.ID. No.311	ORF1072	653053	652397	heat shock protein gpE	PIR:PN0843	8,00E-23
SEQ.ID. No.312	ORF1073	654930	653053	dnaK-type molecular chaperone (Heat shock protein)	PIR:JN0830	0
SEQ.ID. No.313	ORF1077	657994	655916	alpha-xylosidase	TREMBL:NEW.SSO251975_1	2,00E-41
SEQ.ID. No.314	ORF1082	659278	658565	transmembrane transport protein	PIR:T35672	4,00E-21
SEQ.ID. No.315	ORF1085	659548	660555	transcriptional regulatory protein, LacI-family	TREMBL:SCF43_17	2,00E-27
SEQ.ID. No.316	ORF1090	661813	664047	4-alpha-glucanotransferase	PIR:G70928	1,00E-137
SEQ.ID. No.317	ORF1091	664182	665213	transcriptional regulatory protein, LacI-family	TREMBL:SCF43_17	9,00E-27
SEQ.ID. No.318	ORF1094	665376	667187	alpha-1,4-glucosidase	TREMBL:AF105219_2	1,00E-141
SEQ.ID. No.319	ORF1096	668331	667273	ketol-acid reductoisomerase	PIR:D70855	6,00E-96
SEQ.ID. No.320	ORF1097	669803	668754	ketol-acid reductoisomerase	TREMBL:NEW.SC9A4_16	4,00E-98
SEQ.ID. No.321	ORF1098	671520	670003	transmembrane transport protein	PIR:S47743	1,00E-114
SEQ.ID. No.322	ORF1101	673038	671998	SUCROSE OPERON REGULATORY PROTEIN	SWISSPROT:SCRR_STRMU	1,00E-37
SEQ.ID. No.323	ORF1107	676470	674947	sucP-like protein	TREMBL:AF085245_3	1,00E-149
SEQ.ID. No.324	ORF1108	676805	677851	transposase	TREMBL:AP000342_11	1,00E-50

Table I (continued)

Seq. ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ. ID. No.325	ORF1124	683780	682749	transcription regulator, LacI family	TREMBLNEW:SCG22_12	1,00E-40
SEQ. ID. No. 326	ORF1126	685751	683955	alpha-L-arabinofuranosidase	PIR:S55274	1,00E-158
SEQ. ID. No.327	ORF1127	687709	685919	potassium uptake protein	TREMBLNEW:AE004526_1	3,00E-52
SEQ. ID. No.328	ORF1130	688994	687912	Transcriptional regulators of the LacI family	SWISSPROT:SCRR_STRMU	9,00E-34
SEQ. ID. No.329	ORF1138	692525	690945	Unknown	PIRNEW:C82449	1,00E-35
SEQ. ID. No.330	ORF1141	693835	692552	adenylosuccinate synthetase	PIR:T36519	1,00E-165
SEQ. ID. No.331	ORF1143	694051	695115	fructose-bisphosphate	TREMBL:MLCB4_29	1,00E-115
SEQ. ID. No.332	ORF1145	696249	695332	heat shock protein	PIR:F70549	1,00E-64
SEQ. ID. No.333	ORF1147	697893	696445	ferredoxinferredoxin--NADP reductase	TREMBL:SCF15_2	1,00E-110
SEQ. ID. No.334	ORF1148	698024	698863	Unknown	PIR:H70908	5,00E-22
SEQ. ID. No.335	ORF1150	701365	699209	cation-transporting ATPase	PIR:T36946	1,00E-96
SEQ. ID. No.336	ORF1157	703804	701780	periplasmic serine proteinase	PIR:F72359	9,00E43
SEQ. ID. No.337	ORF1162	704221	705531	queuine tRNA-ribosyltransferase	PIR:B69722	7,00E-84
SEQ. ID. No.338	ORF1168	706971	707651	hemolysin III	TREMBL:AB003158_1	8,00E-23
SEQ. ID. No.339	ORF1172	708786	710264	restriction endonuclease	PIR:JQ0759	2,00E45
SEQ. ID. No.340	ORF1173	711545	710277	methyltransferase	PIR:JQ0760	2,00E-83
SEQ. ID. No.341	ORF1178	715545	714565	peptide methionine sulfoxide reductase	PIR:G81243	1,00E-86
SEQ. ID. No.342	ORF1182	718646	716076	Unknown	PIR:C70619	1,00E-23
SEQ. ID. No.343	ORF1188	719290	718646	Unknown	PIR:S28812	6,00E-26
SEQ. ID. No.344	ORF1192	721991	720885	Unknown	PIR:D64900	6,00E-42
SEQ. ID. No.345	ORF1198	723768	723052	Unknown	PIR:S66056	1,00E-35
SEQ. ID. No.346	ORF1208	727984	730425	X-Pro dipeptidyl-peptidase	TREMBLNEW:SC9E12_7	1,00E-127
SEQ. ID. No.347	ORF1210	730613	731311	Unknown	PIR:T36712	7,00E-23
SEQ. ID. No.348	ORF1212	731344	731871	Unknown	PIR:T36713	2,00E-20
SEQ. ID. No.349	ORF1213	731879	733570	phosphoprotein phosphatase	PIR:H70699	2,00E-53

Table I (continued)

Seq. ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ. ID. No.350	ORF1215	733570	735126	FtsW cell division protein	PIR:T36715	6,00E-75
SEQ. ID. No.351	ORF1217	735126	736589	penicillin-binding protein	PIR:F70699	2,00E-87
SEQ. ID. No.352	ORF1220	736589	737536	serine/threonine protein kinase	PIR:E70699	1,00E-55
SEQ. ID. No.353	ORF1221	737536	739605	probable serine/threonine protein kinase	PIR:T36717	1,00E-107
SEQ. ID. No.354	ORF1223	740478	739837	glutamine amidotransferase	PIR:T36720	8,00E-62
SEQ. ID. No.355	ORF1225	741767	740532	Unknown	PIR:T36718	8,00E-28
SEQ. ID. No.356	ORF1228	742564	741767	Unknown	PIR:T36722	1,00E-28
SEQ. ID. No.357	ORF1234	744637	743795	Unknown	PIR:A70840	9,00E-24
SEQ. ID. No.358	ORF1238	747835	745313	Phosphorylase	PIR:S77252	0
SEQ. ID. No.359	ORF1242	749016	750104	tryptophanyl-tRNA synthetase	PIR:E75438	1,00E-58
SEQ. ID. No.360	ORF1244	752072	750288	Unknown	PIR:D75261	5,00E-36
SEQ. ID. No.361	ORF1247	753762	752125	sodium/proline symporter	PIR:H69870	1,00E-91
SEQ. ID. No.362	ORF1256	756161	758911	PHOSPHOENOLPYRUVATE CARBOXYLASE	SWISSPROT:CAPP ANASP	1,00E-100
SEQ. ID. No.363	ORF1266	763670	762024	ATP-dependent DNA helicase	PIR:F75302	3,00E-34
SEQ. ID. No.364	ORF1269	764892	763888	transcription regulator, LacI family	TREMBLNEW:SCG22_12	3,00E-23
SEQ. ID. No.365	ORF1272	765438	766721	permease	TREMBLNEW:AP001515_262	5,00E-65
SEQ. ID. No.366	ORF1274	768757	768844	THIOREDOXIN REDUCTASE	SWISSPROT:TRXB_EUBAC	6,00E-78
SEQ. ID. No.367	ORF1275	769489	768929	alkyl hydrogen peroxide reductase	TREMBL:AF016233_2	9,00E-66
SEQ. ID. No.368	ORF1277	769695	770375	IctA like carbonic anhydrase IctA	PIR:E70804	1,00E-36
SEQ. ID. No.369	ORF1280	770716	771978	hemolysin	PIR:S76248	5,00E-52
SEQ. ID. No.370	ORF1281	772078	772554	Unknown	TREMBL:AF068267_1	4,000-30
SEQ. ID. No.371	ORF1291	775634	776737	Unknown	PIR:164018	1,00E-38
SEQ. ID. No.372	ORF1298	781148	779817	aspartate transaminase	PIR:E71009	8,00E-68
SEQ. ID. No.373	ORF1300	781354	781785	transcriptional regulatory protein	PIR:D70981	1,00E-29
SEQ. ID. No.374	ORF1302	782107	783450	NADP-specific glutamate dehydrogenase	TREMBLNEW:AP001514_107	1,00E-162

Table I (continued)

Seq. ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val.
SEQ. ID. No. 375	ORF1304	785251	783833	Unknown	PIR:D71089	3,00E-67
SEQ. ID. No. 376	ORF1309	789370	786722	DNA topoisomerase chain	PIR:T10970	0
SEQ. ID. No. 377	ORF1310	791528	789441	DNA GYRASE SUBUNIT B	SWISSPROT:GYRB_STRCO	0
SEQ. ID. No. 378	ORF1314	793363	792179	DNA repair and genetic recombination protein	PIR:T10967	7,00E-60
SEQ. ID. No. 379	ORF1315	794566	793445	DNA-directed DNA polymerase III beta chain	PIR:B41870	2,00E-88
SEQ. ID. No. 380	ORF1318	796804	795305	replication initiation protein dnaA	PIR:IQMCL	1,00E-106
SEQ. ID. No. 381	ORF1323	797960	798964	SpolJ like protein	PIR:T36570	9,00E-33
SEQ. ID. No. 382	ORF1325	799091	799621	Unknown	PIR:T36571	2,00E-40
SEQ. ID. No. 383	ORF1327	799776	800438	GLUCOSE-INHIBITED DIVISION PROTEIN B	TREMBL:AF187159_6	3,00E-33
SEQ. ID. No. 384	ORF1328	800652	801659	ATPases involved in chromosome partitioning	TREMBL:AF187159_5	1,00E-76
SEQ. ID. No. 385	ORF1329	801662	803020	partitioning or sporulation protein	PIR:T36574	2,00E-68
SEQ. ID. No. 386	ORF1331	804354	803332	THIOREDOXIN REDUCTASE	SWISSPROT:TRXB_MYCSM	1,00E-82
SEQ. ID. No. 387	ORF1337	808341	806617	Unknown	PIR:T36581	4,00E-44
SEQ. ID. No. 388	ORF1342	812056	810608	MutT/nudix family protein	PIR:E70600	1,00E-28
SEQ. ID. No. 389	ORF1344	811984	813396	RNA nucleotidyltransferase	PIR:T36583	1,00E-162
SEQ. ID. No. 390	ORF1347	815110	814163	Unknown	PIR:F70603	3,00E-26
SEQ. ID. No. 391	ORF1350	816033	815110	dimethyladenosine transferase	PIR:E70603	7,00E-62
SEQ. ID. No. 392	ORF1358	821476	819239	serine/threonine protein kinase	TREMBL:SCL11_7	7,00E-36
SEQ. ID. No. 393	ORF1374	826539	826943	involved in RIBONUCLEOTIDE REDUCTASE FUNCTION	PIR:E70648	1,00E-33
SEQ. ID. No. 394	ORF1376	827062	829254	RIBONUCLEOSIDE-DIPHOSPHATE REDUCTASE ALPHA	SWISSPROT:RIR1_MYCTU	0
SEQ. ID. No. 395	ORF1378	829569	830558	ribonucleotide reductase subunit R2F	PIR:C70861	1,00E-145
SEQ. ID. No. 396	ORF1379	830640	831797	glycosyl transferase (cps like)	PIR:T44648	1,00E-29
SEQ. ID. No. 397	ORF1381	832160	833284	ABC-type sugar transport protein	TREMBL:SRMSIK_1	1,00E-127
SEQ. ID. No. 398	ORF1390	841887	843461	Unknown	PIR:S52348	1,00E-20

Table I (continued)

Seq. ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val.
SEQ. ID. No. 399	ORF1392	843648	844631	fimbria-associated protein	TREMBL:AP019629_2	1,00E-41
SEQ. ID. No. 400	ORF1399	845955	847364	Unknown	TREMBLNEW:SC5F8_10	1,00E-108
SEQ. ID. No. 401	ORF1400	848496	847477	RNA methyltransferase	TREMBLNEW:SCD8A_9	2,00E-51
SEQ. ID. No. 402	ORF1401	848068	849849	permease	TREMBLNEW:SCD46_22	8,00E-50
SEQ. ID. No. 403	ORF1403	849865	850758	beta-1,4-D-xylanase	PIR:S16567	8,00E-35
SEQ. ID. No. 404	ORF1405	850944	853928	cation-transporting ATPase	TREMBLNEW:AP001515_249	1,00E-178
SEQ. ID. No. 405	ORF1407	854346	855527	transposase	TREMBLNEW:AB032203_2	1,00E-48
SEQ. ID. No. 406	ORF1410	855686	856453	cyclase involved in histidine biosynthetic pathway	PIR:T35077	2,00E-96
SEQ. ID. No. 407	ORF1413	856856	858619	anthranilate synthase component I	SWISSPROT:TAPE_ARTGO	1,00E-141
SEQ. ID. No. 408	ORF1415	858938	860536	ABC transporter ATP binding protein	TREMBL:SC18_25	1,00E-179
SEQ. ID. No. 409	ORF1418	861361	861726	Unknown	TREMBL:SCD25_30	9,00E-23
SEQ. ID. No. 410	ORF1421	864063	862453	methyl coenzyme M reductase system, component A2	PIR:D69159	3,00E-67
SEQ. ID. No. 411	ORF1427	866861	865593	transposase	TREMBL:REU010061_1	4,00E-78
SEQ. ID. No. 412	ORF1442	875122	878154	Excinuclease ABC chain A	PIR:S04781	0
SEQ. ID. No. 413	ORF1443	878307	880670	excinuclease abc subunit c	PIR:A70903	3,00E-92
SEQ. ID. No. 414	ORF1445	880782	881750	shikimate 5-dehydrogenase	PIR:D70660	1,00E-25
SEQ. ID. No. 415	ORF1447	881753	882736	Unknown	PIR:T36025	3,00E-80
SEQ. ID. No. 416	ORF1450	882938	883885	Unknown	PIR:D70903	3,00E-65
SEQ. ID. No. 417	ORF1453	883937	885259	phosphoglycerate kinase	PIR:T36019	1,00E-135
SEQ. ID. No. 418	ORF1454	885319	886119	triose phosphate isomerase	PIR:A70916	8,00E-68
SEQ. ID. No. 419	ORF1457	886536	887483	lactate dehydrogenase	PIR:T44580	1,00E-67
SEQ. ID. No. 420	ORF1463	888457	889998	aminotransferase	TREMBL:H132714_11	1,00E-151
SEQ. ID. No. 421	ORF1467	892749	891415	branched-chain amino acid transport system II carrier protein	SWISSPROT:BRNQ_BACSU	1,00E-69
SEQ. ID. No. 422	ORF1469	893981	892881	transaldolase	PIR:C70917	1,00E-108

Table I (continued)

Seq.ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ.ID. No.423	ORF1470	896210	894105	transketolase	PIR:T35162	0
SEQ.ID. No.424	ORF1473	896585	897700	heat-inducible transcriptional repressor	TREMBL:SCC77_22	7,00E-65
SEQ.ID. No.425	ORF1476	897759	898901	heat-shock protein DnaJ	TREMBL:SCC77_21	8,00E-69
SEQ.ID. No.426	ORF1481	899886	900767	bacitracin resistance like protein	TREMBL:NEW:SC2G61_8	3,00E-55
SEQ.ID. No.427	ORF1482	901919	900930	Unknown	PIR:S72871	3,00E-35
SEQ.ID. No.428	ORF1486	902580	904610	threonine-tRNA synthetase	TREMBL:SCL2_21	0
SEQ.ID. No.429	ORF1488	904753	905334	Histidine triad protein (hit)	TREMBL:SCL2_20	1,00E-49
SEQ.ID. No.430	ORF1490	905476	906228	Unknown	PIR:F70500	3,00E-84
SEQ.ID. No.431	ORF1491	906237	906818	probable crossover junction endodeoxyribonuclease ruvC	PIR:A70727	7,00E-32
SEQ.ID. No.432	ORF1493	906879	907502	holliday junction DNA helicase	TREMBL:SCL2_9	7,00E-26
SEQ.ID. No.433	ORF1494	907505	908566	holliday junction DNA helicase	TREMBL:SCL2_8	1,00E-113
SEQ.ID. No.434	ORF1497	909132	909710	Adenine/guanine phosphoribosyltransferases	TREMBL:ECU82864_67	3,00E-32
SEQ.ID. No.435	ORF1499	909810	911009	succinyl-CoA synthetase beta subunit	PIR:T45434	3,00E-92
SEQ.ID. No.436	ORF1501	911012	911920	succinyl-CoA synthetase alpha subunit	PIR:T45435	3,00E-98
SEQ.ID. No.437	ORF1506	913270	914904	5'-phosphoribosyl-5-aminoimidazole-4-carboxamide formyltransferase	TREMBL:AB003159_3	1,00E-166
SEQ.ID. No.438	ORF1512	916418	917185	pseudouridyate synthase	TREMBL:MLCB1351_3	7,00E-64
SEQ.ID. No.439	ORF1514	917185	919311	GTP-binding protein	PIR:H70504	1,00E-143
SEQ.ID. No.440	ORF1515	919669	921195	UDP-glucose pyrophosphorylase	TREMBL:AF203909_1	5,00E-57
SEQ.ID. No.441	ORF1523	923592	926180	helicase	TREMBL:SCI41_14	1,00E-148
SEQ.ID. No.442	ORF1529	929078	928449	hypothetical protein Rv1830 - Mycobacterium	PIR:G70721	3,00E-34
SEQ.ID. No.443	ORF1530	929622	929182	Unknown	TREMBL:NEW:SC1A8A_4	2,00E-28
SEQ.ID. No.444	ORF1531	930450	929632	Unknown	PIR:B70721	4,00E-23
SEQ.ID. No.445	ORF1535	932460	931768	CDP-diacylglycerol-glycerol-3-phosphate 3-phosphatidyltransferase	TREMBL:NEW:SC1A8A_9	4,00E-21
SEQ.ID. No.446	ORF1536	933247	932399	ATP-phosphoribosyl transferase	PIR:D70513	2,00E-73

Table I (continued)

Seq. ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ. ID. No. 447	ORF1540	934253	933588	ribulose-phosphate 3-epimerase	PIR:E70901	2,00E-60
SEQ. ID. No. 448	ORF1541	935276	934332	prolipo protein diacylglycerol transferase	TREMBLNEW:SC8E7_19	1,00E-55
SEQ. ID. No. 449	ORF1545	936264	935392	tryptophan synthase	TREMBL:AF057042_2	2,00E-63
SEQ. ID. No. 450	ORF1546	938369	936285	tryptophan synthase beta chain	PIR:T35066	1,00E-134
SEQ. ID. No. 451	ORF1549	939747	938899	Endonuclease IV	TREMBLNEW:AP001511_275	3,00E-49
SEQ. ID. No. 452	ORF1548	939871	941268	histidine permease	PIR:A69751	1,00E-137
SEQ. ID. No. 453	ORF1559	945113	944658	Unknown	PIR:T35570	8,00E-34
SEQ. ID. No. 454	ORF1575	952215	951598	MUTATOR MUTT. PROTEIN	TREMBLNEW:AP001517_211	7,00E-33
SEQ. ID. No. 455	ORF1580	954360	955931	histidine permease	PIR:A69751	1,00E-151
SEQ. ID. No. 456	ORF1581	956788	956141	signal peptidase I	TREMBL:SLTK245IP_1	6,00E-37
SEQ. ID. No. 457	ORF1587	959688	960875	aspartate aminotransferase	PIR:H69826	2,00E-65
SEQ. ID. No. 458	ORF1590	960918	962678	Unknown	PIR:T35571	5,00E-30
SEQ. ID. No. 459	ORF1595	963514	964434	Unknown	TREMBL:SA17221_1	4,00E-81
SEQ. ID. No. 460	ORF1599	966884	966192	Orotate phosphoribosyltransferase	TREMBLNEW:AE004945_10	8,00E45
SEQ. ID. No. 461	ORF1601	968170	968896	dihydroorotate dehydrogenase	PIR:B70304	1,00E-57
SEQ. ID. No. 462	ORF1604	968691	967870	dihydroorotate dehydrogenase	PIR:G39845	5,00E-23
SEQ. ID. No. 463	ORF1605	969780	968830	orotidine 5'-phosphate decarboxylase	PIR:G75302	3,00E-38
SEQ. ID. No. 464	ORF1607	971294	969801	pyrC DIHYDROOROTASE	SWISSPROT:PYRC_LACPL	4,00E-58
SEQ. ID. No. 465	ORF1611	972690	971713	aspartate carbamoyltransferase, catalytic chain	PIR:C75042	1,00E-79
SEQ. ID. No. 466	ORF1613	976044	972817	glutamate-ammonia-ligase adenyltransferase	PIR:A70776	1,00E-171
SEQ. ID. No. 467	ORF1615	977221	976103	bile salt hydrolase	TREMBLNEW:AF148138_1	0
SEQ. ID. No. 468	ORF1617	978041	977190	5,10-methylenetetrahydrofolate reductase	PIR:D81326	3,00E-56
SEQ. ID. No. 469	ORF1618	980403	978103	5-methyltetrahydropteroylglutamate-- homocystei methyltransferase	PIR:C81326	0
SEQ. ID. No. 470	ORF1622	982368	981301	SAM-dependent methyltransferase	TREMBL:SCI41_34	3,00E-63

Table I (continued)

Seq.ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ. ID. No.471	ORF1627	984644	983910	transcription regulator	TREMBLNEW:AP001516_108	4,00E-38
SEQ. ID. No.472	ORF1631	985704	986210	Unknown	TREMBLNEW:AE004789_1	1,00E-33
SEQ. ID. No.473	ORF1646	992784	993620	Unknown	TREMBLNEW:AF164956_27	2,00E-22
SEQ. ID. No.474	ORF1656	997180	996596	bacterioferritin comigratory protein	PIR:F70870	4,00E-38
SEQ. ID. No.475	ORF1662	1000036	999293	ABC-type transport system	PIR:D70860	5,00E-45
SEQ. ID. No.476	ORF1664	1001554	1000307	hexosyltransferase	TREMBL:SCM11_17	1,00E-105
SEQ. ID. No.477	ORF1670	1005950	1004313	peptide transport system secreted peptide-binding protein	PIR:C70789	1,00E-124
SEQ. ID. No.478	ORF1676	1009609	1008077	glutamate synthase	PIR:T34868	1,00E-151
SEQ. ID. No.479	ORF1678	1014182	1009614	glutamate synthase large chain	PIR:T34869	0
SEQ. ID. No.480	ORF1687	1018227	1017184	Transcriptional regulators of the Lad family	TREMBL:SC6D11_7	1,00E-45
SEQ. ID. No.481	ORF1696	1020864	1021502	Unknown	PIR:F69433	7,00E-20
SEQ. ID. No.482	ORF1697	1022739	1021558	transposase	TREMBLNEW:AB032203_2	1,00E-48
SEQ. ID. No.483	ORF1705	1025143	1023926	Unknown	TREMBLNEW:AE004537_6	2,00E-94
SEQ. ID. No.484	ORF1707	1025240	1026337	transcriptional regulator, LacI-family	TREMBL:AB016845_1	3,00E-36
SEQ. ID. No.485	ORF1708	1027829	1026423	oxygen-independent coproporphyrinogen III oxidase	TREMBL:SCC77_26	1,00E-77
SEQ. ID. No.486	ORF1711	1029709	1027832	lepA"; product: "GTP-binding protein (elongation factor family)	PIR:G70683	0
SEQ. ID. No.487	ORF1715	1031159	1030371	Unknown	PIR:T34761	1,00E-33
SEQ. ID. No.488	ORF1717	1032306	1031410	beta-lactamase regulatory protein	SWISSPROT:YBLI_STRCI	8,00E-26
SEQ. ID. No.489	ORF1719	1033627	1032503	branched-chain amino acid aminotransferase	PIRNEW:A82612	1,00E-103
SEQ. ID. No.490	ORF1721	1034472	1033855	ribosomal protein 125	TREMBLNEW:SCE66_3	2,00E-33
SEQ. ID. No.491	ORF1725	1037559	1036138	NAD(P)+ transhydrogenase (B-specific)	TREMBL:PR05294_3	2,00E-90
SEQ. ID. No.492	ORF1728	1039043	1037883	NAD(P) transhydrogenase	PIR:F70618	3,00E-56
SEQ. ID. No.493	ORF1730	1039384	1041492	long-chain-fatty-acid-CoA ligase	PIR:E70937	1,00E-115
SEQ. ID. No.494	ORF1731	1042669	1041551	GTP-binding protein	PIR:C70586	2,00E-77

Table I (continued)

Seq. ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ. ID. No. 495	ORF1733	1044047	1042617	Unknown	PIR:E70586	8,00E-54
SEQ. ID. No. 496	ORF1737	1044803	1044126	Unknown	TREMBL:SCC117_6	2,00E-24
SEQ. ID. No. 497	ORF1739	1045836	1044664	Phosphate starvation-inducible protein PhoH	TREMBL:SCC117_5	2,00E-83
SEQ. ID. No. 498	ORF1742	1047039	1046245	Unknown	TREMBL:SCC77_19	3,00E-28
SEQ. ID. No. 499	ORF1743	1047283	1048158	rRNA methylase	TREMBL:SCC11_8	2,00E-60
SEQ. ID. No. 500	ORF1745	1048362	1049603	glucose-1-phosphate adenylyltransferase	PIR:C70610	1,00E-122
SEQ. ID. No. 501	ORF1746	1050289	1049699	Unknown	PIR:E70872	3,00E-26
SEQ. ID. No. 502	ORF1747	1050835	1050299	Unknown Function. NifU-related protein	PIR:T35992	1,00E-29
SEQ. ID. No. 503	ORF1749	1052136	1050865	Aminotransferase	PIR:C70872	2,00E-95
SEQ. ID. No. 504	ORF1751	1053054	1052278	ABC-type transport system ATP-binding chain	PIR:T35994	1,00E-100
SEQ. ID. No. 505	ORF1753	1054315	1053083	Unknown	PIR:T35996	4,00E-77
SEQ. ID. No. 506	ORF1754	1055820	1054324	ABC transporter membrane protein	PIR:T35997	0
SEQ. ID. No. 507	ORF1759	1059546	1057888	CTP synthetase	PIR:T36879	0
SEQ. ID. No. 508	ORF1760	1060978	1059695	peptidase V	PIR:B69994	1,00E-30
SEQ. ID. No. 509	ORF1763	1061638	1061195	3-dehydroquinase dehydratase	PIR:F75475	2,00E-33
SEQ. ID. No. 510	ORF1765	1063424	1061805	3-dehydroquinase synthase	TREMBLNEW:SC9C5_18	2,00E-82
SEQ. ID. No. 511	ORF1768	1064694	1063510	chorismate synthase	PIR:H70658	1,00E-117
SEQ. ID. No. 512	ORF1770	1066580	1065402	Unknown	TREMBLNEW:AF170880_2	3,00E-30
SEQ. ID. No. 513	ORF1773	1069739	1067061	alanine-tRNA ligase	PIR:C70520	0
SEQ. ID. No. 514	ORF1779	1071663	1073519	acyltransferase	PIR:C69975	6,00E-57
SEQ. ID. No. 515	ORF1782	1074239	1073616	ribosomal protein	PIR:A37146	8,00E-40
SEQ. ID. No. 516	ORF1783	1075406	1074441	ABC transporter (ATP-binding protein)	TREMBLNEW:AE004665_5	9,00E-39
SEQ. ID. No. 517	ORF1789	1079904	1077262	ATP-dependent DNA helicase	TREMBLNEW:SCD63A_8	0
SEQ. ID. No. 518	ORF1790	1080021	1080599	xanthine phosphoribosyltransferase	TREMBLNEW:AE004942_6	1,00E-45
SEQ. ID. No. 519	ORF1792	1080653	1082014	xanthine/uracil permease family protein	PIR:E81141	6,00E-62

Table I (continued)

Seq. ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ. ID. No.520	ORF1800	1083887	1084822	Unknown	TREMBLNEW:SC9E12_23	3,00E-32
SEQ. ID. No.521	ORF1803	1085474	1086085	nicotinamidase	PIR:B70944	4,00E-40
SEQ. ID. No.522	ORF1811	1091637	1090564	ABC transporter (ATP-binding protein)	TREMBLNEW:AP001514_104	2,00E-58
SEQ. ID. No.523	ORF1819	1093279	1093932	two-component response regulator	PIR:T36862	7,00E-31
SEQ. ID. No.524	ORF1823	1095812	1094763	low-affinity inorganic phosphate transport homolog	PIR:A69855	2,00E-44
SEQ. ID. No.525	ORF1827	1098586	1096190	carbon starvation protein	PIR:H70649	1,00E-170
SEQ. ID. No.526	ORF1829	1098729	1100123	Unknown	TREMBLNEW:AP001517_49	1,00E-34
SEQ. ID. No.527	ORF1834	1103124	1100941	ATP-dependent RNA helicase	TREMBL:SCD25_32	1,00E-100
SEQ. ID. No.528	ORF1836	1104994	1103507	uracil transport protein	PIR:D64842	2,00E-72
SEQ. ID. No.529	ORF1843	1108353	1107193	Unknown	TREMBL:EFY17797_6	1,00E-37
SEQ. ID. No.530	ORF1850	1111209	1112906	serine-threonine protein kinase	PIR:T10009	2,00E-22
SEQ. ID. No.531	ORF1853	1114437	1112950	macrolide-efflux pump	TREMBL:LLLPIK214_12	1,00E-35
SEQ. ID. No.532	ORF1855	1116800	1114752	multidrug resistance protein	PIR:F69763	1,00E-80
SEQ. ID. No.533	ORF1865	1122567	1121476	gtp-binding protein	PIR:F70898	1,00E-121
SEQ. ID. No.534	ORF1866	1123565	1122588	pyrroline-5-carboxylate reductase	PIR:D71281	4,00E-42
SEQ. ID. No.535	ORF1868	1124803	1123463	prolyl aminopeptidase	PIR:JC4823	9,00E-95
SEQ. ID. No.536	ORF1871	1125014	1127587	two-component sensor kinase	PIR:T36078	3,00E-28
SEQ. ID. No.537	ORF1874	1127666	1128409	two-component response regulator	PIR:T29457	5,00E-54
SEQ. ID. No.538	ORF1875	1131146	1128507	Unknown	TREMBLNEW:SCG20A_11	4,00E-35
SEQ. ID. No.539	ORF1880	1131979	1131191	ABC transporter, ATP-binding protein	TREMBLNEW:SCG20A_12	8,00E-72
SEQ. ID. No.540	ORF1885	1133644	1132331	O-acetylhomoserine	TREMBLNEW:AP001516_32	1,00E-126
SEQ. ID. No.541	ORF1888	1134197	1135066	pyridoxal kinase	PIR:G70195	8,00E-24
SEQ. ID. No.542	ORF1891	1135867	1137399	Mg(2+) chelatase family protein	PIR:D70926	1,00E-117
SEQ. ID. No.543	ORF1892	1137399	1130096	DNA processing chain A (DprA) protein	PIR:C70926	4,00E-29
SEQ. ID. No.544	ORF1895	1139156	1141018	succinate dehydrogenase	TREMBLNEW:SC5G8_24	1,00E-138

Table I (continued)

Seq.ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ.ID. No.545	ORF1896	1141117	1142079	fumarate reductase	PIR:F70843	7,00E-35
SEQ.ID. No.546	ORF1899	1143828	1142890	Unknown	TREMBLNEW:SCP8_3	9,00E-69
SEQ.ID. No.547	ORF1901	1145479	1144064	sodium/proton antiporter	PIR:T36685	3,00E-61
SEQ.ID. No.548	ORF1905	1147454	1145964	ATP-dependent ctp proteinase	TREMBL:BSCLPXGEN_1	1,00E-128
SEQ.ID. No.549	ORF1907	1148202	1147504	ATP-dependent protease	TREMBL:AF071885_2	7,00E-67
SEQ.ID. No.550	ORF1908	1148831	1148211	ATP-dependent ctp proteinase	PIR:D70865	9,00E-58
SEQ.ID. No.551	ORF1911	1150898	1149435	chloride channel protein-related protein	TREMBL:AF179611_12	4,00E-26
SEQ.ID. No.552	ORF1914	1152461	1151085	chaperone protein	PIR:E70865	5,00E-83
SEQ.ID. No.553	ORF1915	1153817	1152519	Ribonuclease	PIR:T34708	9,00E-76
SEQ.ID. No.554	ORF1918	1155396	1154518	pyruvate formate-lyase 1 activating enzyme	TREMBL:AF088897-13	8,00E-54
SEQ.ID. No.555	ORF1920	1157920	1155509	formate C-acetyltransferase	TREMBL:AF088897_12	0
SEQ.ID. No.556	ORF1922	1160121	1158427	NAD+ synthase (glutamine-hydrolyzing)	PIRNEW:T51756	1,00E-128
SEQ.ID. No.557	ORF1923	1161621	1160473	hippurate hydrolase	PIR:E69640	5,00E-75
SEQ.ID. No.558	ORF1928	1163598	1162396	ABC transporter (ATP-binding protein)	TREMBLNEW:AP001518_312	7,00E-77
SEQ.ID. No.559	ORF1930	1164712	1163735	lipoprotein	PIR:JN0753	4,00E-36
SEQ.ID. No.560	ORF1932	1164914	1165732	Unknown	PIR:C69862	2,00E-24
SEQ.ID. No.561	ORF1935	1168334	1165860	transketolase I	PIR:S76896	0
SEQ.ID. No.562	ORF1936	1168735	1170339	GMP synthetase	PIR:A70735	0
SEQ.ID. No.563	ORF1939	1170918	1172789	acetyltransferase	PIR:C69975	3,00E-57
SEQ.ID. No.564	ORF1941	1172869	1173897	ribose-phosphate pyrophosphokinase	PIR:D70622	1,00E-113
SEQ.ID. No.565	ORF1943	1174182	1175561	udp-n-acetylglucosamine pyrophosphorylase -	PIR:E70622	1,00E-110
SEQ.ID. No.566	ORF1944	1175568	1175978	Unknown	TREMBL:SCC123_15	9,00E-28
SEQ.ID. No.567	ORF1946	1176163	1176858	phosphoglycerate mutase	PIR:A75439	2,00E-20
SEQ.ID. No.568	ORF1949	1177491	1179188	phosphate acetyltransferase	PIR:F70628	2,00E-95
SEQ.ID. No.569	ORF1951	1179326	1180552	ACETATE KINASE	SWISSPROT:ACKA_CORGL	1,00E-104

Table I (continued)

Seq.ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ.ID. No.570	ORF1952	1182093	1180729	3-phosphoshikimate 1-carboxyvinyltransferase	TREMBLNEW:SC7E4_9	2,00E-89
SEQ.ID. No.571	ORF1957	1183623	1184213	resolvase	PIR:A70583	2,00E-34
SEQ.ID. No.572	ORF1959	1184203	1185522	transposase	PIR:B70583	6,00E-47
SEQ.ID. No.573	ORF1962	1188391	1186907	lactose transport protein	TREMBL:LL47655_2	1,00E-132
SEQ.ID. No.574	ORF1964	1188756	1191824	beta-galactosidase	TREMBL:BLO242596_1	0
SEQ.ID. No.575	ORF1967	1192641	1193192	3-methyladenine-DNA glycosylase	TREMBL:BLO242596_2	1,00E-108
SEQ.ID. No.576	ORF1972	1197131	1194993	glycosyl hydrolase	TREMBL:SCO001206_2	0
SEQ.ID. No.577	ORF1976	1201862	1198998	DNA polymerase I	PIR:C70559	0
SEQ.ID. No.578	ORF1977	1202693	1201911	response regulator	PIR:T35758	3,00E-50
SEQ.ID. No.579	ORF1980	1205315	1203789	pyruvate kinase	PIR:T35759	1,00E-130
SEQ.ID. No.580	ORF1982	1206382	1205399	transmembrane transport protein	PIR:T36036	2,00E-72
SEQ.ID. No.581	ORF1983	1208662	1206554	excinuclease ABC chain B	PIR:S03812	0
SEQ.ID. No.582	ORF1984	1209291	1208677	Unknown	PIR:T35741	7,00E-35
SEQ.ID. No.583	ORF1986	1210940	1209468	ribosomal protein S1	PIR:T35743	0
SEQ.ID. No.584	ORF1988	1211938	1211063	methylene tetrahydrofolate dehydrogenase	TREMBLNEW:SC2A6_9	1,00E-85
SEQ.ID. No.585	ORF1991	1213312	1214295	ABC transporter, ATP-binding protein	TREMBLNEW:AP001511_283	7,00E-24
SEQ.ID. No.586	ORF1995	1214365	1215195	permease of ABC zinc transporter	TREMBLNEW:AE004962_10	4,00E-25
SEQ.ID. No.587	ORF1997	1215774	1215253	Unknown	PIR:C70607	3,00E-27
SEQ.ID. No.588	ORF1999	1216476	1215886	transcription factor	PIR:H70803	7,00E-46
SEQ.ID. No.589	ORF2002	1216693	1218903	1,4-alpha-glucan branching enzyme	PIR:B70770	0
SEQ.ID. No.590	ORF2003	1218942	1219661	phosphate response regulator protein phoP	TREMBLNEW:SCCB12_7	4,00E-79
SEQ.ID. No.591	ORF2005	1219661	1220734	two-component system sensor kinase	TREMBLNEW:SCCB12_6	3,00E-45
SEQ.ID. No.592	ORF2021	1228492	1229922	transcription regulator	PIR:T35584	2,00E-24
SEQ.ID. No.593	ORF2025	1230170	1231918	cell division-related protein	TREMBLNEW:SCD35_15	6,00E-40
SEQ.ID. No.594	ORF2029	1233918	1232389	Sensory transduction histidine kinase	PIR:E70596	2,00E-73

Table I (continued)

Seq.ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ. ID. No.595	ORF2033	1235060	1235875	hemolysin-like protein	TREMBL:AB003158_1	5,00E-33
SEQ. ID. No.596	ORF2037	1236412	1235936	transcription elongation factor	PIR:F70894	7,00E-22
SEQ. ID. No.597	ORF2038	1236918	1236514	peptidylprolyl isomerase	PIR:S46228	2,00E-25
SEQ. ID. No.598	ORF2039	1239279	1237083	L-serine dehydratase	PIR:T34749	1,00E-128
SEQ. ID. No.599	ORF2043	1240667	1239669	exopolyphosphatase	PIR:E70623	1,00E-53
SEQ. ID. No.600	ORF2045	1241296	1240733	Unknown	PIR:D70623	1,00E-30
SEQ. ID. No.601	ORF2048	1243293	1241998	phosphopyruvate hydratase	PIR:B69620	1,00E-140
SEQ. ID. No.602	ORF2050	1244391	1243447	oxidoreductase	PIR:B75341	3,00E-32
SEQ. ID. No.603	ORF2053	1248115	1244534	transcription-repair coupling factor (mfd)	PIR:G70622	0
SEQ. ID. No.604	ORF2055	1248704	1248108	peptidyl-tRNA hydrolase	PIR:A70622	2,00E-36
SEQ. ID. No.605	ORF2061	1251010	1250516	phosphothioic acetyltransferase	PIR:E75427	2,00E-21
SEQ. ID. No.606	ORF2062	1254333	1251136	Unknown	TREMBLNEW:SC23B6_28	1,00E-160
SEQ. ID. No.607	ORF2065	1256591	1255809	Unknown	TREMBL:SCC123_17	3,00E-69
SEQ. ID. No.608	ORF2068	1258578	1257169	gamma-glutamyl phosphate	TREMBL:SCC123_23	1,00E-109
SEQ. ID. No.609	ORF2070	1259284	1258586	glycine hydroxymethyltransferase	PIR:C70896	9,00E-41
SEQ. ID. No.610	ORF2071	1259507	1260994	threonine synthase	PIR:T39213	7,00E-73
SEQ. ID. No.611	ORF2074	1261517	1264300	cation-transporting P-ATPase	PIR:E69000	1,00E-144
SEQ. ID. No.612	ORF2078	1266735	1265818	ABC transporter, ATP-binding protein	TREMBLNEW:AP001509_90	5,00E-52
SEQ. ID. No.613	ORF2082	1269816	1268017	DNA repair protein	PIR:T36883	3,00E-88
SEQ. ID. No.614	ORF2087	1270844	1269819	Unknown	PIR:T36884	4,00E-59
SEQ. ID. No.615	ORF2091	1271091	1272554	potassium uptake protein KtrB	TREMBLNEW:AP001509_36	2,00E-47
SEQ. ID. No.616	ORF2094	1272191	1273267	potassium uptake protein KtrA	TREMBLNEW:AP001509_35	1,00E-30
SEQ. ID. No.617	ORF2097	1274906	1274067	Hemolysin A homolog	PIR:T36885	8,00E-47
SEQ. ID. No.618	ORF2099	1276134	1275097	sugar phosphatase	PIR:T36891	1,00E-59
SEQ. ID. No.619	ORF2102	1277930	1276146	Unknown	PIR:B70502	2,00E-27

Table I (continued)

Seq. ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ. ID. No.620	ORF2106	1279280	1277961	tyrosyl-tRNA synthetase	TREMBL:SCI8_3	1,00E-122
SEQ. ID. No.621	ORF2113	1282087	1281281	molybdopterln biosynthesis protein	PIR:A70415	3,00E-75
SEQ. ID. No.622	ORF2115	1283033	1282167	thiamin biosynthesis protein	PIR:B81307	2,00E-71
SEQ. ID. No.623	ORF2119	1285060	1283591	argininosuccinate lyase	TREMBL:SCI24_6	1,00E-153
SEQ. ID. No.624	ORF2120	1286744	1285509	argininosuccinate synthase	PIR:JC4548	1,00E-152
SEQ. ID. No.625	ORF2122	1287429	1286830	arginine repressor	TREMBL:SCI24_12	3,00E-28
SEQ. ID. No.626	ORF2123	1288301	1287339	ornithine carbamoyltransferase	PIR:C70621	6,00E-96
SEQ. ID. No.627	ORF2125	1289640	1288348	acetonitrile aminotransferase	TREMBL:SCI24_13	1,00E-75
SEQ. ID. No.628	ORF2126	1290586	1289633	acetylglutamate kinase	PIR:A70621	2,00E-84
SEQ. ID. No.629	ORF2127	1291833	1290661	glutamate N-acetyltransferase	PIR:H70620	2,00E-85
SEQ. ID. No.630	ORF2128	1292924	1291833	N-acetyl-gamma-glutamyl-phosphate reductase	PIR:T36815	3,00E-80
SEQ. ID. No.631	ORF2133	1296349	1293743	phenylalanyl-tRNA synthetase beta chain	PIR:T36829	1,00E-171
SEQ. ID. No.632	ORF2135	1297424	1296360	phenylalanyl-tRNA synthetase alpha chain	PIR:T36830	1,00E-87
SEQ. ID. No.633	ORF2137	1298362	1297481	rRNA methylase	PIR:T36832	1,00E-32
SEQ. ID. No.634	ORF2141	1300779	1299379	cation ABC transporter (ATP-binding protein)	PIR:H69858	3,00E-70
SEQ. ID. No.635	ORF2145	1303117	1301753	peptidase	PIR:G70870	3,00E-92
SEQ. ID. No.636	ORF2150	1303979	1305466	dihydropyrimidine dehydrogenase	PIR:JC4089	1,00E-72
SEQ. ID. No.637	ORF2154	1306655	1308088	glutamine synthetase I	TREMBL:CGGLNA_1	0
SEQ. ID. No.638	ORF2159	1310751	1310080	GALACTOSIDE O-ACETYLTRANSFERASE	SWISSPROT:THGA_LACLA	4,00E-47
SEQ. ID. No.639	ORF2161	1311605	1310916	endonuclease III related protein	PIR:A64479	2,00E-30
SEQ. ID. No.640	ORF2162	1312971	1311616	Unknown	TREMBL:NEWAP001514_169	7,00E-53
SEQ. ID. No.641	ORF2166	1315626	1313032	exonuclease ABC chain A	TREMBL:SCM10_6	1,00E-124
SEQ. ID. No.642	ORF2186	1323905	1322865	alcohol dehydrogenase (Zn-dependent)	PIR:T44975	6,00E-81
SEQ. ID. No.643	ORF2201	1330127	1328892	translation elongation factor EF-Tu	PIR:D26956	1,00E-159
SEQ. ID. No.644	ORF2203	1332384	1330264	translation elongation factor EF-G	PIR:E70827	0

Table 1 (continued)

Seq.ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ. ID. No.645	ORF2207	1335090	1334032	sodium-dependent transporter	PIR:E69902	4,00E-70
SEQ. ID. No.646	ORF2211	1335424	1336674	low specificity L-threonine aldolase	PIR:T02833	3,00E-68
SEQ. ID. No.647	ORF2215	1337984	1336827	polysaccharide biosynthesis protein	PIR:D71867	1,00E-60
SEQ. ID. No.648	ORF2217	1338152	1339492	phosphoribosylglycinamide formyltransferase 2	TREMBLNEW:AE004794_3	1,00E-100
SEQ. ID. No.649	ORF2220	1339888	1340637	phosphoribosylaminoimidazole succinocarboxamide synthetase	TREMBLNEW:AP001509_64	7,00E-68
SEQ. ID. No.650	ORF2223	1340703	1344434	phosphoribosylformylglycinamide synthase	PIRNEW:A82272	6,00E-45
SEQ. ID. No.651	ORF2225	1344328	1345869	lipase/esterase	PIR:C69484	1,00E-28
SEQ. ID. No.652	ORF2239	1350691	1351665	potassium channel, beta subunit	PIR:A75289	5,00E-71
SEQ. ID. No.653	ORF2241	1353512	1351920	Unknown	TREMBL:AF188935_69	2,00E-30
SEQ. ID. No.654	ORF2242	1353671	1355170	adenosylhomocysteinase	PIR:B72649	3,00E-59
SEQ. ID. No.655	ORF2250	1358226	1359185	amino acid ABC transporter, permease protein	PIR:H69278	3,00E-23
SEQ. ID. No.656	ORF2251	1359185	1359967	glutamine transport protein	PIR:H69334	7,00E-67
SEQ. ID. No.657	ORF2253	1360374	1361882	amidophosphoribosyltransferase	PIRNEW:T51702	0
SEQ. ID. No.658	ORF2254	1361951	1363039	phosphoribosylaminoimidazole synthetase	TREMBLNEW:AP001509_69	1,00E-117
SEQ. ID. No.659	ORF2256	1363069	1364334	phosphoribosylamine-glycine ligase	TREMBL:LLJ000883_2	1,00E-130
SEQ. ID. No.660	ORF2258	1366348	1364714	aldehyde dehydrogenase (NAD(P)+)	SWISSPROT:DHAP_HUMAN	1,00E-83
SEQ. ID. No.661	ORF2260	1368544	1366472	Unknown	PIR:T00092	2,00E-66
SEQ. ID. No.662	ORF2263	1369728	1368808	Unknown	PIR:D70507	1,00E-22
SEQ. ID. No.663	ORF2265	1370680	1370243	metal uptake regulation protein	TREMBL:SCC121_11	5,00E-31
SEQ. ID. No.664	ORF2266	1371855	1370680	phosphoribosylaminoimidazole carboxylase	TREMBL:LLJ000883_4	1,00E-102
SEQ. ID. No.665	ORF2269	1372345	1371842	phosphoribosylaminoimidazole carboxylase	PIR:DEBSPE	4,00E-52
SEQ. ID. No.666	ORF2270	1373433	1372444	NADPH:quinone oxidoreductase	PIRNEW:T51766	1,00E-42
SEQ. ID. No.667	ORF2271	1373472	1375793	1-deoxyxylulose-5-phosphate synthase	PIR:E70528	3,00E-64
SEQ. ID. No.668	ORF2277	1379299	1378547	ABC transporter, ATP-binding protein	PIR:B69377	3,00E-56

Table I (continued)

Seq. ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ. ID. No. 669	ORF2283	1382045	1380999	transcriptional regulator	SWISSPROT:Y143_HAEIN	2,00E-24
SEQ. ID. No. 670	ORF2284	1381963	1384269	arabinosidase	TREMBL:BO15178_1	3,00E-65
SEQ. ID. No. 671	ORF2288	1385925	1384741	Unknown	PIR:B64819	7,00E-24
SEQ. ID. No. 672	ORF2292	1387407	1386478	Asparaginase	PIR:D64820	3,00E-49
SEQ. ID. No. 673	ORF2294	1389427	1387766	aminotransferase	PIR:E75208	5,00E-67
SEQ. ID. No. 674	ORF2297	1390405	1389488	hisH-like amidotransferase	TREMBL:SCL2_12	4,00E-38
SEQ. ID. No. 675	ORF2299	1391180	1390212	superoxide-inducible protein	PIR:F64173	1,00E-113
SEQ. ID. No. 676	ORF2300	1393384	1391279	DNA primase	TREMBL:AF027507_3	1,00E-125
SEQ. ID. No. 677	ORF2301	1394975	1393551	deoxyguanosinetriphosphate triphosphohydrolase	TREMBL:SC7A8_9	1,00E-108
SEQ. ID. No. 678	ORF2302	1396385	1395030	alanine racemase	PIR:T35574	8,00E-73
SEQ. ID. No. 679	ORF2304	1396598	1398031	amino acid transporter	PIR:E69825	1,00E-145
SEQ. ID. No. 680	ORF2307	1399425	1399009	Unknown	PIR:T43793	1,00E-24
SEQ. ID. No. 681	ORF2309	1401568	1399616	DNA helicase recQ	PIR:F69901	1,00E-117
SEQ. ID. No. 682	ORF2312	1404774	1403593	CYSTATHIONINE GAMMA-SYNTHASE	SWISSPROT:METB_MYCLE	1,00E-126
SEQ. ID. No. 683	ORF2313	1406092	1404889	cystathionine beta-synthase	TREMBL:NEW:SCE25_18	1,00E-110
SEQ. ID. No. 684	ORF2316	1407402	1406422	oligopeptide transport protein	PIR:S75333	1,00E-43
SEQ. ID. No. 685	ORF2318	1407988	1407200	oligopeptide transport ATP-binding protein	PIR:G75026	3,00E-47
SEQ. ID. No. 686	ORF2319	1409343	1407988	PEPTIDE ABC TRANSPORTER PERMEASE	SWISSPROT:Y4TQ_RHISN	3,00E-32
SEQ. ID. No. 687	ORF2322	1409861	1408887	oligopeptide	PIR:G64820	5,00E-35
SEQ. ID. No. 688	ORF2324	1411545	1409929	probable oligopeptide binding protein	PIR:B71130	7,00E-39
SEQ. ID. No. 689	ORF2326	1411671	1412438	Unknown	TREMBL:NEW:AP001507_86	1,00E-46
SEQ. ID. No. 690	ORF2327	1413877	1412504	solute-binding lipoprotein	TREMBL:SC6D11_4	6,00E-79
SEQ. ID. No. 691	ORF2329	1415381	1414041	solute-binding lipoprotein	TREMBL:SC6D11_4	1,00E-104
SEQ. ID. No. 692	ORF2333	1417065	1415716	solute-binding protein/sugar-binding protein	TREMBL:SC6D11_4	2,00E-91
SEQ. ID. No. 693	ORF2334	1417225	1418922	alpha-L-arabinofuranosidase	TREMBL:NEW:AP001513_134	1,00E-124

Table I (continued)

Seq. ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ. ID. No. 694	ORF2335	1420082	1419048	transcription regulator, LacI family	TREMBL:NEW:SCG22_12	9,00E-61
SEQ. ID. No. 695	ORF2337	1422258	1420186	beta-galactosidase	TREMBL:SC6D11_3	0
SEQ. ID. No. 696	ORF2341	1423483	1422476	ABC transporter sugar permease	TREMBL:SC6D11_5	1,00E-116
SEQ. ID. No. 697	ORF2342	1424471	1423542	ABC-type sugar transport systems	TREMBL:SC6D11_6	1,00E-77
SEQ. ID. No. 698	ORF2343	1424688	1425695	transcription regulator, LacI family	TREMBL:SC6D11_7	2,00E-68
SEQ. ID. No. 699	ORF2346	1426592	1427404	Unknown	SWISSPROT:Y4ME_RHISN	4,00E-25
SEQ. ID. No. 700	ORF2347	1428151	1427463	Unknown	PIR:F70533	9,00E-45
SEQ. ID. No. 701	ORF2350	1430120	1428231	glucosamine-fructose-6-phosphate aminotransferase	PIR:T35569	0
SEQ. ID. No. 702	ORF2362	1431192	1430365	glutamine transport protein	TREMBL:AF104994_3	1,00E-75
SEQ. ID. No. 703	ORF2354	1432191	1431211	amino acid ABC transporter, peptidase protein	TREMBL:NEW:SC27G11_21	2,00E-50
SEQ. ID. No. 704	ORF2366	1433263	1432325	periplasmic amino acid-binding protein	TREMBL:NEW:SC27G11_22	7,00E-36
SEQ. ID. No. 705	ORF2357	1434481	1433400	Periplasmic amino acid binding protein	TREMBL:NEW:SC27G11_22	2,00E-42
SEQ. ID. No. 706	ORF2358	1435112	1434516	SSRA-BINDING PROTEIN	TREMBL:SCE59_25	5,00E-45
SEQ. ID. No. 707	ORF2362	1437540	1436620	cell division protein (ftsX)	TREMBL:SCE59_27	3,00E-40
SEQ. ID. No. 708	ORF2363	1438721	1437555	cell division ATP-binding protein	TREMBL:SCE59_28	6,00E-71
SEQ. ID. No. 709	ORF2364	1439854	1438733	translation releasing factor RF-2	TREMBL:SCE59_31	1,00E-126
SEQ. ID. No. 710	ORF2369	1442368	1441718	polypeptide deformylase	TREMBL:SCM1_16	4,00E-41
SEQ. ID. No. 711	ORF2371	1443778	1442396	phospho-sugar mutase	PIR:T35565	1,00E-117
SEQ. ID. No. 712	ORF2377	1448432	1445826	ALANINE AMINOPEPTIDASE	TREMBL:SC8E4A_13	0
SEQ. ID. No. 713	ORF2378	1450387	1448477	D-ala-D-ala dipeptidase	PIR:T35845	0
SEQ. ID. No. 714	ORF2380	1451314	1450412	dihydrodipicolinate synthase	PIR:H70879	1,00E-64
SEQ. ID. No. 715	ORF2381	1452232	1451480	dihydrodipicolinate reductase	PIR:D70882	1,00E-57
SEQ. ID. No. 716	ORF2384	1453887	1452571	transport protein	PIR:T35894	8,00E-41
SEQ. ID. No. 717	ORF2388	1458334	1454102	ATP-dependent DNA helicase	PIR:G70951	2,00E-61
SEQ. ID. No. 718	ORF2399	1462569	1463987	probable serine/threonine-specific protein kinase	PIR:A70652	8,00E-35

Table I (continued)

Seq.ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ. ID. No.719	ORF2409	1469810	1471522	methanol dehydrogenase regulatory protein	TREMBLNEW:AP001509_42	3,00E-84
SEQ. ID. No.720	ORF2422	1481598	1477564	DNA-directed RNA polymerase	PIR:G70535	0
SEQ. ID. No.721	ORF2423	1485329	1481769	DNA-directed RNA polymerase	PIR:F70535	0
SEQ. ID. No.722	ORF2425	1487257	1486274	adenine glycosylase	PIR:T36366	1,00E-60
SEQ. ID. No.723	ORF2428	1487191	1487937	rRNA methylase	PIR:E70971	2,00E-40
SEQ. ID. No.724	ORF2432	1489611	1488250	Unknown	PIRNEW:E81818	1,00E-161
SEQ. ID. No.725	ORF2434	1491352	1490105	galactokinase	TREMBLNEW:SCE66_15	6,00E-77
SEQ. ID. No.726	ORF2436	1492631	1491372	galactose-1-phosphate uridylyltransferase	TREMBLNEW:SCE66_17	5,00E-68
SEQ. ID. No.727	ORF2438	1493508	1492616	Transcription regulator DeoR family	TREMBLNEW:SCG20A_6	1,00E-49
SEQ. ID. No.728	ORF2441	1493917	1494930	probable dihydroorotate oxidase (EC 1.3.3.1) -	PIR:S76039	2,00E-44
SEQ. ID. No.729	ORF2443	1496474	1495104	NADH-dependent flavin oxidoreductase	PIR:H75303	5,00E-85
SEQ. ID. No.730	ORF2446	1498981	1496869	penicillin-binding protein	PIR:T36565	2,00E-61
SEQ. ID. No.731	ORF2449	1499804	1499088	transcription regulator	PIR:T36556	3,00E-50
SEQ. ID. No.732	ORF2450	1501128	1500046	lipoate protein ligase	PIR:T46883	3,00E-67
SEQ. ID. No.733	ORF2452	1502217	1501189	3-ISOPROPYLMALATE DEHYDROGENASE	SWISSPROT:LEU3_CORGL	1,00E-107
SEQ. ID. No.734	ORF2453	1504798	1502285	peptidase	PIR:A70709	2,00E-93
SEQ. ID. No.735	ORF2459	1507988	1506699	Unknown	PIR:E70951	1,00E-34
SEQ. ID. No.736	ORF2465	1509811	1510179	thioredoxin	TREMBL:SCM1_18	9,00E-22
SEQ. ID. No.737	ORF2472	1514695	1513262	capsular polysaccharide biosynthesis (epsB-like)	PIR:G70066	3,00E-27
SEQ. ID. No.738	ORF2479	1517945	1519261	abortive phage resistance protein	TREMBL:ILLU94520_1	2,00E-23
SEQ. ID. No.739	ORF2489	1524075	1523317	transposase	PIR:T14971	2,00E-37
SEQ. ID. No.740	ORF2494	1525555	1524539	transposase	TREMBLNEW:AP001520_222	5,00E-57
SEQ. ID. No.741	ORF2499	1529926	1528511	dTDP-glucose-4,6-dehydratase	TREMBL:AF030360_3	1,00E-113
SEQ. ID. No.742	ORF2500	1529909	1531084	UDP-galactopyranose mutase	PIR:E70888	1,00E-124

Table I (continued)

Seq. ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ. ID. No. 743	ORF2503	1532593	1533468	2-hydroxyhepta-2,4-diene-1,7-dioate isomerase	PIR:T29076	5,00E-53
SEQ. ID. No. 744	ORF2505	1534592	1533720	transcriptional regulator	TREMBLNEW:AE004771_5	8,00E-26
SEQ. ID. No. 745	ORF2507	1534838	1536388	histidine ammonia-lyase	PIR:JC1172	1,00E-149
SEQ. ID. No. 746	ORF2509	1536610	1539276	endopeptidase ClpB (ATP-binding chain B)	PIR:T36551	0
SEQ. ID. No. 747	ORF2512	1539396	1540532	glutamyl-tRNA synthetase-related protein	PIR:C81210	3,00E-34
SEQ. ID. No. 748	ORF2515	1542345	1541869	Unknown	PIR:H70090	1,00E-45
SEQ. ID. No. 749	ORF2517	1543019	1542396	uracil phosphoribosyltransferase	TREMBLNEW:AP001519_279	1,00E-52
SEQ. ID. No. 750	ORF2519	1543338	1544645	Unknown	TREMBL:AF179376_1	9,00E-57
SEQ. ID. No. 751	ORF2523	1546932	1545721	MutT 1-like	PIR:F70673	2,00E-27
SEQ. ID. No. 752	ORF2528	1549312	1547078	polyphosphate kinase	PIR:E70673	0
SEQ. ID. No. 753	ORF2532	1552013	1551240	transcription regulator	PIR:T29082	3,00E-82
SEQ. ID. No. 754	ORF2535	1552331	1553731	3-Isopropylmalate dehydratase	PIR:T29083	1,00E-178
SEQ. ID. No. 755	ORF2536	1553817	1554506	3-Isopropylmalate dehydratase	PIR:T45426	9,00E-64
SEQ. ID. No. 756	ORF2542	1556552	1557664	Dihydroorotate oxidase	PIR:A23559	2,00E-41
SEQ. ID. No. 757	ORF2544	1559219	1557876	NADH oxidase	PIR:S26965	1,00E-114
SEQ. ID. No. 758	ORF2546	1559468	1560790	UDP-N-acetylglucosamine transferase	TREMBL:SCOE59_8	1,00E-162
SEQ. ID. No. 759	ORF2547	1562095	1560845	Aminotransferase	PIR:D70849	4,00E-57
SEQ. ID. No. 760	ORF2549	1563499	1562192	lysR type transcription regulator	PIR:T35595	7,00E-31
SEQ. ID. No. 761	ORF2552	1564473	1563211	Multidrug resistance protein	PIR:D72388	7,00E-27
SEQ. ID. No. 762	ORF2556	1565361	1567220	arginine-tRNA ligase	PIR:H70772	1,00E-147
SEQ. ID. No. 763	ORF2557	1567226	1568815	Diaminopimelate decarboxylase	PIR:S03827	2,00E-56
SEQ. ID. No. 764	ORF2559	1568979	1570292	Homoserine dehydrogenase	PIR:B70773	1,00E-101
SEQ. ID. No. 765	ORF2561	1570402	1571511	HOMOSERINE KINASE	SWISSPROT:KHSE_BRELA	1,00E-34
SEQ. ID. No. 766	ORF2562	1571651	1573096	mat-like protein	PIR:S76166	6,00E-29
SEQ. ID. No. 767	ORF2565	1573295	1574365	ABC transporter ATP-binding protein	TREMBLNEW:SCK7_8	8,00E-60

Table I (continued)

Seq.ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ. ID. No. 768	ORF2572	1576911	1578242	succinyl-diaminopimelate desuccinylase	TREMBL:NEW:SCP8_2	5,00E-87
SEQ. ID. No. 769	ORF2575	1578592	1581590	cytosolic axial filament protein	TREMBL:SCC88_10	1,00E-158
SEQ. ID. No. 770	ORF2578	1582393	1584081	GTP-binding protein obg	TREMBL:SGD916_3	1,00E-133
SEQ. ID. No. 771	ORF2579	1584085	1585215	Glutamate 5-kinase	TREMBL:SCC123_25	1,00E-78
SEQ. ID. No. 772	ORF2581	1585309	1586511	aspartate transaminase	PIR:T11786	1,00E-132
SEQ. ID. No. 773	ORF2584	1587015	1587905	Transcription antitermination factor	PIR:SS4717	7,00E-48
SEQ. ID. No. 774	ORF2587	1588618	1589307	Ribosomal protein L1	PIR:F70613	3,00E-71
SEQ. ID. No. 775	ORF2605	1596209	1595385	Dehydrogenase	PIR:D69988	2,00E-78
SEQ. ID. No. 776	ORF2606	1596341	1597789	Xylulokinase	PIR:S18582	1,00E-54
SEQ. ID. No. 777	ORF2608	1598182	1599594	Histidinol dehydrogenase	PIR:S26209	1,00E-122
SEQ. ID. No. 778	ORF2609	1599594	1600751	Histidinol-phosphate transaminase	PIR:JQ0637	1,00E-90
SEQ. ID. No. 779	ORF2610	1600840	1601438	Imidazole glycerol-phosphate dehydratase	PIR:C70544	4,00E-65
SEQ. ID. No. 780	ORF2613	1602268	1602912	Glutamine amidotransferase	PIR:JQ0640	3,00E-55
SEQ. ID. No. 781	ORF2616	1602985	1603707	N-(5'-phospho-D-ribosylformimino)-5-amino-1-(5"-phosphoribosyl)-4-imidazolealboxamide isomerase	PIR:JQ0641	2,00E-79
SEQ. ID. No. 782	ORF2617	1605571	1603817	Unknown	PIR:T34645	6,00E-96
SEQ. ID. No. 783	ORF2618	1605396	1606730	Glutamine synthetase	TREMBL:SC1G2_3	1,00E-175
SEQ. ID. No. 784	ORF2626	1612686	1608481	ATP-dependent helicase	TREMBL:SCD25_28	0
SEQ. ID. No. 785	ORF2628	1613260	1612607	Unknown	PIR:F69751	4,00E-31
SEQ. ID. No. 786	ORF2630	1613419	1614921	ATP/GTP-binding protein	PIR:T35116	1,00E-117
SEQ. ID. No. 787	ORF2631	1615084	1616064	L-lactate dehydrogenase	PIR:JQ0183	0
SEQ. ID. No. 788	ORF2632	1617147	1616212	cation efflux system protein	PIR:T35276	7,00E-41
SEQ. ID. No. 789	ORF2635	1618038	1617316	SOS response regulator	TREMBL:SCAJ4870_2	3,00E-62
SEQ. ID. No. 790	ORF2637	1618556	1619029	Unknown	TREMBL:SCAJ4870_3	3,00E-52

Table 1 (continued)

Seq. ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ. ID. No. 791	ORF2638	1620366	1619170	D-3-phosphoglycerate dehydrogenase	PIRNEW:C82072	1,00E-111
SEQ. ID. No. 792	ORF2639	1622656	1620380	helicase protein	TREMBL:SC6A11_15	1,00E-113
SEQ. ID. No. 793	ORF2641	1622989	1623507	Unknown	TREMBLNEW:AP001516_5	2,00E-29
SEQ. ID. No. 794	ORF2642	1623510	1624586	Unknown	PIR:T34962	3,00E-79
SEQ. ID. No. 795	ORF2647	1625042	1626841	cell division protein	TREMBL:AF123319_2	9,00E-70
SEQ. ID. No. 796	ORF2652	1627792	1629240	UDP-N-acetylmuramoylalanine-D-glutamyl-2,6-diaminopimelate-D-alanyl-alanyl ligase	PIR:T34958	6,00E-75
SEQ. ID. No. 797	ORF2653	1629288	1630391	phospho-N-acetylmuramoyl-pentapeptide-transferase	PIR:T34957	3,00E-80
SEQ. ID. No. 798	ORF2655	1630449	1631891	UDP-N-acetylmuramoylalanine-D-glutamate ligase	PIR:T34956	1,00E-81
SEQ. ID. No. 799	ORF2657	1631737	1633095	cell division protein ftsW	PIR:T34955	6,00E-41
SEQ. ID. No. 800	ORF2661	1633114	1634292	UDP-N-acetylglucosamine-N-acetylmuramyl-(pentapeptide) pyrophosphoryl-undecaprenol N-acetylglucosamine transferase	PIR:T34954	1,00E-87
SEQ. ID. No. 801	ORF2662	1634396	1635931	UDP-N-acetylmuramoyl-L-alanine ligase	PIR:T35852	2,00E-78
SEQ. ID. No. 802	ORF2671	1638807	1638253	Unknown	PIRNEW:F82517	1,00E-20
SEQ. ID. No. 803	ORF2674	1639338	1639811	Unknown	TREMBLNEW:AF276071_1	3,00E-34
SEQ. ID. No. 804	ORF2676	1639975	1643091	alpha-mannosidase	TREMBL:SCM11_3	0
SEQ. ID. No. 805	ORF2677	1642913	1646362	alpha-mannosidase	TREMBL:SCM11_3	0
SEQ. ID. No. 806	ORF2678	1646635	1649736	alpha-mannosidase	TREMBL:SCM11_3	0
SEQ. ID. No. 807	ORF2685	1649935	1651203	solute-binding protein/sugar-binding protein	TREMBL:SCM11_7	3,00E-91
SEQ. ID. No. 808	ORF2686	1651209	1652144	lactose transport system permease protein	TREMBL:SCM11_6	6,00E-70
SEQ. ID. No. 809	ORF2687	1652147	1653001	sugar ABC transporter, permease protein	TREMBL:SCM11_5	5,00E-61
SEQ. ID. No. 810	ORF2688	1653018	1654304	Unknown	TREMBL:SCM11_4	1,00E-101
SEQ. ID. No. 811	ORF2689	1654432	1657071	alpha-xylosidase	TREMBLNEW:SS0251975_1	8,00E45
SEQ. ID. No. 812	ORF2691	1657008	1659932	cation-transporting ATPase	TREMBLNEW:AP001509_223	1,00E-177

Table I (continued)

Seq. ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ. ID. No. 813	ORF2693	1660231	1661334	transcription regulator, LacI family	TREMBL:SCM11_8	2,00E-59
SEQ. ID. No. 814	ORF2695	1662757	1661482	Unknown	PIR:S40824	6,00E-83
SEQ. ID. No. 815	ORF2697	1664059	1662764	unknown	TREMBL:NEW:AP001509_228	1,00E-108
SEQ. ID. No. 816	ORF2701	1666453	1665242	transcriptional regulator, ROK family	PIR:NEW:A82130	3,00E-36
SEQ. ID. No. 817	ORF2704	1666680	1667591	glucose kinase	PIR:B69632	9,00E-26
SEQ. ID. No. 818	ORF2706	1668868	1667747	Transcriptional regulators of NagC/XylR family	TREMBL:NEW:AP001516_187	4,00E-31
SEQ. ID. No. 819	ORF2709	1669206	1670015	glucosamine 6-phosphate isomerase	TREMBL:NEW:SC7E4_33	6,00E-85
SEQ. ID. No. 820	ORF2710	1669981	1671354	N-acetylglucosamine 6-phosphate deacetylase	PIR:C70845	7,00E-55
SEQ. ID. No. 821	ORF2713	1671637	1673268	oligopeptide binding protein	TREMBL:SCI41_38	9,00E-86
SEQ. ID. No. 822	ORF2715	1673436	1674524	oligopeptide ABC transporter, permease protein	PIR:A72289	3,00E-48
SEQ. ID. No. 823	ORF2719	1674646	1675695	dipeptide ABC transporter, permease protein (dppC)	PIR:H69470	7,00E-33
SEQ. ID. No. 824	ORF2722	1675702	1677408	ABC transporter/ATP-binding protein	TREMBL:ECD720_13	1,00E-116
SEQ. ID. No. 825	ORF2724	1679626	1678034	X-Pro aminopeptidase	PIR:JN0491	1,00E-108
SEQ. ID. No. 826	ORF2729	1682035	1683621	folypolyglutamate synthase	TREMBL:SCC88_25	7,00E-99
SEQ. ID. No. 827	ORF2730	1683685	1687359	chromosome segregation SMC protein	PIR:T35661	0
SEQ. ID. No. 828	ORF2734	1690151	1688601	UDP-N-acetylmuramoylalanine-D-glutamate-2,6-diaminopimelate ligase	PIR:T34959	1,00E-28
SEQ. ID. No. 829	ORF2736	1690269	1691075	RNA polymerase sigma factor	PIR:T42015	1,00E-37
SEQ. ID. No. 830	ORF2740	1692608	1691687	aldose epimerase family protein	PIR:540823	3,00E-29
SEQ. ID. No. 831	ORF2742	1693689	1692736	Unknown	PIR:S40823	1,00E-22
SEQ. ID. No. 832	ORF2744	1693914	1694969	penicillin tolerance protein LytB	PIR:D70898	9,00E-89
SEQ. ID. No. 833	ORF2745	1695449	1695015	Unknown	PIR:T35087	4,00E-26
SEQ. ID. No. 834	ORF2747	1696673	1695618	glyceraldehyde 3-phosphate dehydrogenase	PIR:T09633	1,00E-116
SEQ. ID. No. 835	ORF2753	1699247	1699879	translation initiation factor IF-3	PIR:T36835	3,00E-47
SEQ. ID. No. 836	ORF2754	1700110	1700490	ribosomal protein L20	PIR:T36833	4,00E-50
SEQ. ID. No. 837	ORF2755	1700608	1701531	integrase/recombinase	PIR:D70503	4,00E-70

Table I (continued)

Seq.ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ.ID. No.838	ORF2757	1701682	1704505	ABC transporter ATP binding subunit	TREMBL:U73183_1	1,00E-106
SEQ. ID. No.839	ORF2759	1704710	1705606	partitioning or sporulation protein	PIR:T36875	2,00E-82
SEQ. ID. No.840	ORF2761	1705628	1706539	Unknown	PIR:T36873	1,00E-40
SEQ. ID. No.841	ORF2762	1706555	1707268	Unknown	PIR:T36872	6,00E46
SEQ.ID. No.842	ORF2764	1707403	1708227	MutT/nudix family protein	PIR:S75926	1,00E-30
SEQ.ID. No.843	ORF2767	1708291	1708568	quinolinate synthetase A	TREMBLNEW:AP001511_109	1,00E-104
SEQ.ID. No.844	ORF2769	1709659	1711287	L-aspartate oxidase	PIR:T36393	4,00E-83
SEQ.ID. No.845	ORF2770	1711294	1712184	nicotinate-nucleotide pyrophosphorylase	PIRNEW:T51326	2,00E-60
SEQ.ID. No.846	ORF2772	1712178	1713434	cysteine desulfurase	TREMBLNEW:AF276772_1	3,00E-61
SEQ.ID. No.847	ORF2776	1713469	1714815	transport protein	PIR:C69757	4,00E-70
SEQ.ID. No.848	ORF2778	1715133	1717061	GTP-binding translation elongation factor	PIR:F70556	0
SEQ. ID. No.849	ORF2784	1718661	1719725	oxidoreductase	PIR:C70800	1,00E-24
SEQ. ID. No.850	ORF2788	1720232	1721302	integrase/recombinase	TREMBL:MLCB250_62	2,00E-61
SEQ.ID. No.851	ORF2790	1721558	1723195	peptide transport system secreted peptide-binding protein	PIR:C70789	1,00E-111
SEQ. ID. No.852	ORF2793	1723499	1724227	peptidetransport system permease.-	PIR:B70789	5,00E-67
SEQ.ID. No.853	ORF2795	1724443	1725444	oligopeptide ABC transporter (permease)	TREMBLNEW:SC9E12_4	9,00E-71
SEQ. ID. No.854	ORF2797	1725470	1727476	peptidetransport system ABC-transporter	PIR:H70788	1,00E-119
SEQ. ID. No.855	ORF2798	1727584	1728441	exodeoxyribonuclease	TREMBL:SCE87_25	2,00E-58
SEQ. ID. No.856	ORF2803	1729382	1730137	Unknown	PIR:T34826	1,00E-21
SEQ. ID. No.857	ORF2806	1730091	1731395	RNA methyltransferase	PIR:T34574	4,00E-43
SEQ. ID. No.858	ORF2810	1732196	1734706	Integral membrane ATPase	PIR:T36308	1,00E-144
SEQ.ID. No.859	ORF2811	1734830	1737526	aconitate hydratase	PIR:F70873	0
SEQ. ID. No.860	ORF2820	1742368	1741469	two-component response regulator	TREMBL:SCAH10_19	1,00E-33
SEQ. ID. No.861	ORF2826	1744819	1745715	Unknown	PIR:B64815	1,00E-36

Table I (continued)

Seq. ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ. ID. No. 862	ORF2831	1745858	1745871	Unknown	TREMBLNEW:AE004781_1	5,00E-42
SEQ. ID. No. 863	ORF2832	1747749	1748910	GTP-pyrophosphokinase	TREMBLNEW:AP001513_158	2,00E-43
SEQ. ID. No. 864	ORF2833	1747791	1749230	Unknown	PIR:T35107	1,00E-148
SEQ. ID. No. 865	ORF2834	1749061	1750227	tRNA delta(2)-isopentenylpyrophosphate	PIR:T35111	2,00E-72
SEQ. ID. No. 866	ORF2838	1751033	1754131	ftsK homolog - DNA translocase	PIR:T35683	0
SEQ. ID. No. 867	ORF2840	1754287	1754943	CDPdiacylglycerol-glycerol-3-phosphate 3-phosphatidyltransferase	PIR:572934	1,00E-27
SEQ. ID. No. 868	ORF2847	1758712	1757902	RecA protein	TREMBL:AF094756_1	0
SEQ. ID. No. 869	ORF2852	1759378	1760037	Unknown	PIR:C70592	2,00E-23
SEQ. ID. No. 870	ORF2853	1760202	1763093	preprotein translocase secA	PIR:S71922	0
SEQ. ID. No. 871	ORF2858	1764350	1765393	anthranilate phosphoribosyltransferase	PIR:T35529	5,00E-68
SEQ. ID. No. 872	ORF2864	1766541	1767242	acyltransferase	TREMBL:SC124_2	2,00E-48
SEQ. ID. No. 873	ORF2865	1769570	1767300	serine/threonine-specific protein kinase	TREMBLNEW:AF233851_2	5,00E-61
SEQ. ID. No. 874	ORF2868	1770832	1769717	polyprenyl synthase - like protein	TREMBL:SGCRTB_1	4,00E-20
SEQ. ID. No. 875	ORF2872	1771868	1773289	transcription initiation factor sigma	PIR:T35194	1,00E-140
SEQ. ID. No. 876	ORF2873	1773350	1775665	DNA gyrase chain B	PIR:T35196	1,00E-143
SEQ. ID. No. 877	ORF2876	1777135	1778094	ribokinase	TREMBLNEW:AE004621_9	5,00E-50
SEQ. ID. No. 878	ORF2877	1778113	1782843	ATP-dependent helicase	PIR:G64922	0
SEQ. ID. No. 879	ORF2879	1786819	1783793	DNA gyrase	PIR:T35872	0
SEQ. ID. No. 880	ORF2880	1786749	1788035	Unknown	PIR:T35880	2,00E-48
SEQ. ID. No. 881	ORF2886	1789591	1790084	deoxyuridine 5'-triphosphate nucleotidohydrolase	PIR:T34820	3,00E-42
SEQ. ID. No. 882	ORF2888	1790180	1792522	GTP pyrophosphokinase	PIR:S70687	0
SEQ. ID. No. 883	ORF2890	1793527	1792646	Transposase	TREMBL:ECIS1397_2	2,00E-46
SEQ. ID. No. 884	ORF2895	1794657	1794112	peptidylprolyl isomerase	PIRNEW:T51359	3,00E-35
SEQ. ID. No. 885	ORF2901	1797008	1796076	Unknown	PIR:E71174	3,00E-23

Table I (continued)

Seq. ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ. ID. No. 886	ORF2905	1799082	1799924	phosphoglycerate mutase	PIR:F70685	2,00E-22
SEQ. ID. No. 887	ORF2908	1800042	1800989	transport protein	PIR:A75272	2,00E-50
SEQ. ID. No. 888	ORF2909	1801007	1801930	glutamate-binding periplasmic protein	PIR:T35146	1,00E-32
SEQ. ID. No. 889	ORF2911	1801976	1804936	leucyl-tRNA synthetase	TREMBL:SCC123_9	0
SEQ. ID. No. 890	ORF2914	1805942	1807627	competence-like protein	TREMBL:SCC123_5	2,00E-22
SEQ. ID. No. 891	ORF2916	1807770	1809113	Unknown	TREMBL:NEW:AP001517_57	2,00E-37
SEQ. ID. No. 892	ORF2920	1809279	1810151	Unknown	TREMBL:SCC123_2	2,00E-35
SEQ. ID. No. 893	ORF2921	1810175	1810738	Unknown	PIR:T35576	1,00E-20
SEQ. ID. No. 894	ORF2927	1812252	1813292	O-sialoglycoprotein endopeptidase	PIR:T35581	1,00E-105
SEQ. ID. No. 895	ORF2930	1813962	1814894	Integrase/recombinase	PIR:B70965	3,00E-25
SEQ. ID. No. 896	ORF2951	1824277	1822820	Unknown	TREMBL:NEW:SK7_2	2,00E-22
SEQ. ID. No. 897	ORF2957	1825368	1828001	DNA topoisomerase III topB	PIR:H69724	9,00E-86
SEQ. ID. No. 898	ORF2965	1830496	1829231	type II site-specific deoxyribonuclease	PIR:A34919	2,00E-34
SEQ. ID. No. 899	ORF2968	1831513	1830545	site-specific DNA-methyltransferase (cytosine-specific)	PIR:XYECP2	2,00E-88
SEQ. ID. No. 900	ORF2975	1835344	1833872	Unknown	SWISSPROT:Y4ME_RHISN	4,00E-33
SEQ. ID. No. 901	ORF2984	1839447	1837642	Unknown	PIR:T36167	7,00E-58
SEQ. ID. No. 902	ORF3031	1863238	1858430	aggregation protein precursor	PIR:H41662	5,00E-28
SEQ. ID. No. 903	ORF3041	1866693	1866103	plasmid partition protein	TREMBL:AF121000_6	1,00E-24
SEQ. ID. No. 904	ORF3055	1871346	1872032	Unknown	PIR:F70925	3,00E-20
SEQ. ID. No. 905	ORF3059	1875342	1873996	isocitrate dehydrogenase	PIR:B70846	1,00E-179
SEQ. ID. No. 906	ORF3060	1875134	1876462	IMP dehydrogenase	TREMBL:AB003154_2	1,00E-91
SEQ. ID. No. 907	ORF3062	1877209	1879293	long-chain-fatty-acid-CoA ligase	PIR:E70937	1,00E-111
SEQ. ID. No. 908	ORF3063	1879303	1879788	polypeptide deformylase	PIR:C70631	2,00E-24
SEQ. ID. No. 909	ORF3066	1880103	1880990	ribosomal protein S2	PIR:T34809	2,00E-87
SEQ. ID. No. 910	ORF3067	1881072	1881920	translation elongation factor EF-Ts	PIR:D70925	8,00E-53

Table I (continued)

Seq.ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ.ID. No.911	ORF3069	1882097	1882834	uridylylate kinase	PIR:T34811	7,00E-74
SEQ.ID. No.912	ORF3071	1882914	1883462	ribosome recycling factor	PIR:T35471	5,00E-55
SEQ.ID. No.913	ORF3072	1883386	1884471	phosphatidate cytidylyltransferase	PIR:T35470	6,00E-27
SEQ.ID. No.914	ORF3074	1884685	1885851	Unknown	PIR:T35453	1,00E-113
SEQ.ID. No.915	ORF3075	1886403	1885858	pfpI like protease	TREMBLNEW:AE004833_9	3,00E-37
SEQ.ID. No.916	ORF3078	1886612	1887793	ransposase	TREMBLNEW:AB032203_2	1,00E-48
SEQ.ID. No.917	ORF3083	1890162	1889584	dCTP deaminase	PIR:T36613	4,00E-72
SEQ.ID. No.918	ORF3091	1895286	1893217	Na ⁺ /H ⁺ antiporter	PIR:E70040	2,00E-55
SEQ.ID. No.919	ORF3095	1895982	1898285	alpha-galactosidase	TREMBL:AF124596_1	0
SEQ.ID. No.920	ORF3097	1899661	1898456	transcriptional repressor	TREMBL:SCG11A_2	1,00E-21
SEQ.ID. No.921	ORF3098	1899592	1901121	sugar transport system (sugar-binding protein)	PIR:B42400	4,00E-28
SEQ.ID. No.922	ORF3101	1901146	1902072	membrane protein	PIR:C42400	2,00E-50
SEQ.ID. No.923	ORF3103	1902094	1902957	multiple sugar-binding transport system permease protein	PIR:D42400	6,00E-48
SEQ.ID. No.924	ORF3107	1904376	1906193	oligo-1,6-glucosidase	PIR:A41707	1,00E-163
SEQ.ID. No.925	ORF3108	1906482	1907726	threonine dehydratase	PIR:D72386	8,00E-76
SEQ.ID. No.926	ORF3109	1908525	1907878	SIR2 family transcription regulator	PIR:A72370	4,00E-31
SEQ.ID. No.927	ORF3128	1915770	1916519	transcriptional regulator	TREMBL:CZA382_19	2,00E-20
SEQ.ID. No.928	ORF3129	1917495	1916632	Unknown	TREMBL:SC4A7_14	6,00E-24
SEQ.ID. No.929	ORF3139	1921801	1923762	acyl-CoA carboxylase complex A chain	TREMBL:AF126429_1	1,00E-129
SEQ.ID. No.930	ORF3140	1923758	1925377	propionyl-CoA carboxylase complex B chain	PIR:T42208	1,00E-150
SEQ.ID. No.931	ORF3141	1925419	1934934	fatty-acid synthase	PIR:S55505	0
SEQ.ID. No.932	ORF3162	1944074	1942971	gene: "tnpA"; product: "transposase";	TREMBL:AF052750_3	1,00E-41
SEQ.ID. No.933	ORF3168	1944695	1947220	endo-1,4-beta-xylanase xynD	PIR:H69735	1,00E-120

Table 1 (continued)

Seq.ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ. ID. No.934	ORF3172	1947446	1950319	endo-1,4-beta-xylanase	PIR:T30909	9,00E-95
SEQ. ID. No.935	ORF3181	1952286	1955024	polynucleotide nucleotidyltransferase	PIR:T10932	0
SEQ. ID. No.936	ORF3184	1956848	1955457	Unknown	TREMBLNEW:AP001509_46	2,00E-81
SEQ. ID. No.937	ORF3189	1958007	1958720	ribosomal protein	PIR:S32238	6,00E-48
SEQ. ID. No.938	ORF3205	1966792	1966046	5-formyltetrahydrofolate cyclo-ligase	TREMBL:SCE87_34	2,00E-23
SEQ. ID. No.939	ORF3206	1966819	1967511	Unknown	PIR:F70601	9,00E-24
SEQ. ID. No.940	ORF3211	1969192	1969482	chaperonin groES	TREMBL:AF071828_1	1,00E-30
SEQ. ID. No.941	ORF3214	1971682	1970162	cystathionine gamma-synthase homolog	PIR:T21246	1,00E-65
SEQ. ID. No.942	ORF3221	1972559	1973656	UDP-N-acetylpyruvoylglucosamine reductase	PIR:E70743	2,00E-42
SEQ. ID. No.943	ORF3222	1973811	1975334	cationic amino acid transporter-	PIR:G70593	1,00E-119
SEQ. ID. No.944	ORF3225	1975833	1977065	aminotransferase	PIR:B70876	6,00E-55
SEQ. ID. No.945	ORF3226	1978441	1977098	DNA-DAMAGE-INDUCIBLE PROTEIN PimpB/mucB/samB family protein	PIRNEW:A81861	8,00E-47
SEQ. ID. No.946	ORF3231	1980080	1981420	Unknown	TREMBL:SCM10_29	2,00E-41
SEQ. ID. No.947	ORF3234	1981497	1982510	dehydrogenase	PIRNEW:F82068	8,00E-30
SEQ. ID. No.948	ORF3243	1984135	1986297	4-ALPHA-GLUCANOTRANSFERASE	PIR:G70928	1,00E-139
SEQ. ID. No.949	ORF3247	1987170	1987658	ribosomal protein	PIR:T35564	1,00E44
SEQ. ID. No.950	ORF3248	1990292	1987755	glycosyl hydrolase	TREMBL:SC3D11_13	1,00E-137
SEQ. ID. No.951	ORF3250	1991482	1990292	N-acetylglucosamine repressor	TREMBL:AB009593_3	5,00E-20
SEQ. ID. No.952	ORF3254	1991997	1994723	ALCOHOL DEHYDROGENASE 2	SWISSPROT:ADH2_ENTHI	0
SEQ. ID. No.953	ORF3259	1996645	1997283	ribosomal protein L3	PIR:H70641	4,00E-51
SEQ. ID. No.954	ORF3260	1997293	1997946	ribosomal protein L4	PIR:A70642	3,00E-56
SEQ. ID. No.955	ORF3261	1997955	1998248	ribosomal protein L23	PIR:T45366	5,00E-25
SEQ. ID. No.956	ORF3262	1998288	1999115	ribosomal protein L2	PIR:C70642	1,00E-116

Table I (continued)

Seq.ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ. ID. No.957	ORF3263	1999134	1999409	ribosomal protein	PIR:T45368	2,00E-42
SEQ. ID. No.958	ORF3265	1999791	2000591	ribosomal protein S3	PIR:F70642	4,00E-74
SEQ. ID. No.959	ORF3266	2000601	2001017	ribosomal protein L16 rplP	PIR:G70642	5,00E-48
SEQ. ID. No.960	ORF3270	2002331	2002900	Ribosomal protein L5	PIR:S29884	7,00E-68
SEQ. ID. No.961	ORF3273	2003596	2004132	ribosomal protein L6	PIR:S50001	1,00E-46
SEQ. ID. No.962	ORF3274	2004137	2004505	ribosomal protein L18	PIR:S29887	1,00E-37
SEQ. ID. No.963	ORF3276	2004535	2005233	30S RIBOSOMAL PROTEIN S5.	SWISSPROT:RS5_STRCO	4,00E-50
SEQ. ID. No.964	ORF3279	2005430	2005879	Ribosomal protein	PIR:S29890	8,00E43
SEQ. ID. No.965	ORF3280	2006156	2007490	preprotein translocase	PIR:JC4288	1,00E-137
SEQ. ID. No.966	ORF3282	2007663	2008220	adenylate kinase	PIR:S17070	2,00E46
SEQ. ID. No.967	ORF3288	2009848	2010840	DNA-directed RNA polymerase alpha chain	PIR:F70565	1,00E-134
SEQ. ID. No.968	ORF3289	2010943	2011473	ribosomal protein L17	PIR:T35559	8,00E-36
SEQ. ID. No.969	ORF3290	2012469	2011561	pseudouridylyl synthase	PIR:T35560	6,00E-54
SEQ. ID. No.970	ORF3292	2012670	2014922	Unknown	PIR:C75323	1,00E-102
SEQ. ID. No.971	ORF3294	2015132	2015929	Unknown	PIR:F75328	4,00E-21
SEQ. ID. No.972	ORF3298	2016508	2018307	alpha-L-arabinofuranosidase	PIR:S55274	1,00E-158
SEQ. ID. No.973	ORF3301	2018843	2019883	Transcriptional regulators of the LacI family	TREMBL:NEW:SCG22_12	1,00E-39
SEQ. ID. No.974	ORF3304	2020863	2021927	transcription termination-antitermination factor	PIR:D70588	5,00E-78
SEQ. ID. No.975	ORF3305	2022200	2025061	translation Initiation factor IF-2	PIR:B70694	0
SEQ. ID. No.976	ORF3306	2025217	2025687	ribosome-binding factor A	PIR:T35987	1,00E-24
SEQ. ID. No.977	ORF3308	2025578	2026852	tRNA pseudouridine synthase	PIR:T35986	4,00E-53
SEQ. ID. No.978	ORF3310	2026953	2028074	probable riboflavin kinase (FAD synthetase)	PIR:T35984	8,00E-35
SEQ. ID. No.979	ORF3312	2029630	2028095	DNA repair protein	PIR:T36362	1,00E-111
SEQ. ID. No.980	ORF3316	2031522	2030827	ribose 5-phosphate isomerase	PIR:G69180	2,00E-35
SEQ. ID. No.981	ORF3320	2034810	2033179	mercury(II) reductase	PIR:H64756	1,00E-57

Table I (continued)

Seq. ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ. ID. No. 982	ORF3327	2039100	2037427	phosphoglucumutase	TREMBL:SC6D11_39	1,00E-180
SEQ. ID. No. 983	ORF3328	2040740	2039190	D-xylose proton-symporter	TREMBL:AF045552_3	1,00E-96
SEQ. ID. No. 984	ORF3330	2041240	2043612	glucose permease	TREMBL:AF045481_1	1,00E-120
SEQ. ID. No. 985	ORF3331	2043633	2044469	transcription antiterminalator	PIR:S47216	9,00E-38
SEQ. ID. No. 986	ORF3335	2045875	2047194	seryl-tRNA synthase	PIR:T36067	1,00E-129
SEQ. ID. No. 987	ORF3339	2048203	2049516	sugar-binding protein	TREMBL:SCF91_20	3,00E-35
SEQ. ID. No. 988	ORF3341	2049659	2050678	ABC transporter sugar permease	TREMBL:SC6D11_6	2,00E-50
SEQ. ID. No. 989	ORF3343	2050681	2051628	ABC transporter sugar permease	TREMBL:SC6D11_5	3,00E-53
SEQ. ID. No. 990	ORF3347	2054134	2055210	Unknown	PIR:S77134	7,00E-53
SEQ. ID. No. 991	ORF3351	2055260	2056804	galactose-1-phosphate uridylyltransferase	TREMBL:AF082008_2	6,00E-72
SEQ. ID. No. 992	ORF3354	2056876	2057895	UDPglucose 4-epimerase	PIR:D69628	1,00E-102
SEQ. ID. No. 993	ORF3355	2058841	2057949	two-component system regulator	PIR:T35501	2,00E-27
SEQ. ID. No. 994	ORF3368	2068722	2067535	chloramphenicol resistance protein homolog	TREMBL:ECU73857_115	3,00E-66
SEQ. ID. No. 995	ORF3372	2069223	2070902	lysine-tRNA ligase	PIR:G70954	1,00E-148
SEQ. ID. No. 996	ORF3373	2070967	2071929	1,4-dihydroxy-2-naphthoate octaprenyltransferase	PIR:A70546	1,00E-26
SEQ. ID. No. 997	ORF3374	2071962	2072729	phosphoglycerate mutase	PIR:S30886	9,00E-84
SEQ. ID. No. 998	ORF3376	2073765	2073094	phosphate transport system regulatory protein PhoU-like	PIR:G70533	2,00E-26
SEQ. ID. No. 999	ORF3378	2073780	2075147	Sensory transduction histidine kinases	TREMBL:NEW.SCD8A_2	1,00E-46
SEQ. ID. No. 1000	ORF3381	2076802	2075663	phosphoserine aminotransferase	PIR:T45349	1,00E-110
SEQ. ID. No. 1001	ORF3383	2077196	2078149	Unknown	TREMBL:STH243106_4	3,00E-20
SEQ. ID. No. 1002	ORF3392	2081808	2082683	thymidylate synthase	PIR:C70881	1,00E-109
SEQ. ID. No. 1003	ORF3393	2082514	2083455	dihydrofolate reductase	TREMBL:AF006616_1	3,00E-26
SEQ. ID. No. 1004	ORF3395	2083582	2084097	protein-tyrosine-phosphatase	PIR:T37174	8,00E-22
SEQ. ID. No. 1005	ORF3397	2085624	2084611	branched-chain amino acid transport protein	PIR:G69592	5,00E-74
SEQ. ID. No. 1006	ORF3400	2086942	2085851	Unknown	PIR:G65081	1,00E-30

Table I (continued)

Seq. ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ. ID. No. 1007	ORF3403	2087036	2088046	UDP-glucose 4-epimerase	TREMBL:NEW:AP001510_283	1,00E-61
SEQ. ID. No. 1008	ORF3408	2090294	2088993	cyclopropane-fatty-acyl-phospholipid synthase	TREMBL:MLCB2407_16	3,00E-98
SEQ. ID. No. 1009	ORF3410	2090734	2091882	lactaldehyde reductase	PIR:RDECLA	1,00E-120
SEQ. ID. No. 1010	ORF3413	2092840	2094621	Unknown	PIR:T35137	1,00E-45
SEQ. ID. No. 1011	ORF3419	2094624	2095844	glycosyltransferase	TREMBL:PPRMP_7	2,00E-25
SEQ. ID. No. 1012	ORF3420	2095942	2096895	ABC transporter, ATP-binding protein	TREMBL:NEW:SCD10_29	2,00E-69
SEQ. ID. No. 1013	ORF3423	2098591	2100078	Unknown	PIR:T36334	4,00E-32
SEQ. ID. No. 1014	ORF3426	2100171	2101334	Unknown	PIR:T36332	1,00E-45
SEQ. ID. No. 1015	ORF3428	2101324	2101884	hypoxanthine phosphoribosyltransferase	PIR:T36331	5,00E-40
SEQ. ID. No. 1016	ORF3429	2101884	2103971	cell division protein ftsH2	PIR:T36330	0
SEQ. ID. No. 1017	ORF3431	2104069	2104665	GTP cyclohydrolase I	PIR:T36329	3,00E-64
SEQ. ID. No. 1018	ORF3434	2104731	2105803	Dihydropteroate synthase - Streptomyces	PIR:T36324	3,00E-49
SEQ. ID. No. 1019	ORF3437	2105717	2107126	hydroxymethylidihydropteridine	PIR:T36327	1,00E-30
SEQ. ID. No. 1020	ORF3441	2108830	2107934	acyl-CoA thioesterase II	PIR:NEW:A82248	6,00E-39
SEQ. ID. No. 1021	ORF3443	2110821	2109145	ABC transporter ATP-binding protein	PIR:D70857	0
SEQ. ID. No. 1022	ORF3448	2111654	2112601	glucose kinase	PIR:S26208	9,00E-67
SEQ. ID. No. 1023	ORF3449	2113495	2112632	ABC-transport system ATP binding protein	PIR:T35675	4,00E-57
SEQ. ID. No. 1024	ORF3450	2114702	2113536	transcription repressor	PIR:T35673	4,000-74
SEQ. ID. No. 1025	ORF3454	2114954	2116108	multiple sugar-binding protein	TREMBL:SC4A7_32	1,00E-68
SEQ. ID. No. 1026	ORF3455	2116212	2117762	L-arabinose transport ATP binding protein	TREMBL:AF160811_1	1,00E-168
SEQ. ID. No. 1027	ORF3457	2117765	2118979	L-arabinose membrane permease	TREMBL:AF160811_2	1,00E-71
SEQ. ID. No. 1028	ORF3460	2120072	2120491	permease	TREMBL:OOE250422_3	9,00E-20
SEQ. ID. No. 1029	ORF3461	2120502	2120918	Polypeptide deformylase	TREMBL:CBFMS_1	7,00E-32
SEQ. ID. No. 1030	ORF3466	2123521	2124867	xylose isomerase	PIR:JC1137	0
SEQ. ID. No. 1031	ORF3468	2125136	2126410	transposase	PIR:H70582	1,00E-153

Table I (continued)

Seq. ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ. ID. No. 1032	ORF3473	2129364	2127847	xylulokinase	PIR:A41339	2,00E-78
SEQ. ID. No. 1033	ORF3476	2129584	2130810	Transcriptional regulators of NegC/XyIR family	TREMBLNEW:SCG22_6	1,00E-39
SEQ. ID. No. 1034	ORF3479	2131508	2132593	translation releasing factor RF-1	TREMBLNEW:SC26G5_4	1,00E-105
SEQ. ID. No. 1035	ORF3481	2132883	2133564	Methylase	TREMBLNEW:SC26G5_5	3,00E49
SEQ. ID. No. 1036	ORF3483	2133840	2135024	branched chain amino acid ABC transporter, periplasmic	PIR:C72290	9,00E-41
SEQ. ID. No. 1037	ORF3484	2135269	2136192	high-affinity branched-chain amino acid transport protein	PIR:JH0688	4,00E-51
SEQ. ID. No. 1038	ORF3485	2136212	2137285	branched-chain amino acid transport protein	TREMBLNEW:AE004904_4	6,00E-35
SEQ. ID. No. 1039	ORF3487	2137285	2138142	branched chain amino acid ABC transporter, ATP-binding protein	PIR:F72290	6,00E-71
SEQ. ID. No. 1040	ORF3488	2138145	2138846	branched chain amino acid ABC transporter, ATP-binding protein	PIR:T35757	7,00E-76
SEQ. ID. No. 1041	ORF3490	2139658	2138984	galactoside O-acetyltransferase	PIR:T37905	4,00E-26
SEQ. ID. No. 1042	ORF3493	2139833	2140504	Unknown	PIR:T44498	2,00E-23
SEQ. ID. No. 1043	ORF3495	2140621	2141784	UNDECAPRENYL-PHOSPHATE ALPHA-N-ACETYLGLUCOSAMINYLTRANSFERASE	PIR:T09982	7,00E-49
SEQ. ID. No. 1044	ORF3497	2141756	2143390	Inosine-5'-monophosphate dehydrogenase	PIR:H70736	1,00E-164
SEQ. ID. No. 1045	ORF3499	2143561	2144208	oligoribonuclease	TREMBLNEW:AB036424_2	6,00E-51
SEQ. ID. No. 1046	ORF3500	2144260	2145675	helicase	PIRNEW:T47241	9,00E-53
SEQ. ID. No. 1047	ORF3502	2145719	2147515	Unknown	PIR:D70376	2,00E-20
SEQ. ID. No. 1048	ORF3505	2147505	2148674	pyruvate formate-lyase activating enzyme	PIR:C70646	1,00E-108
SEQ. ID. No. 1049	ORF3509	2149420	2151261	prolyl-tRNA synthetase	PIR:H70588	1,00E-175
SEQ. ID. No. 1050	ORF3513	2154603	2152369	zinc metalloproteinase	PIR:C70838	1,00E-165
SEQ. ID. No. 1051	ORF3518	2155887	2158886	methionine aminopeptidase	PIR:T34903	1,00E-65
SEQ. ID. No. 1052	ORF3517	2156943	2158232	citrate synthase	PIR:E70782	1,00E-124
SEQ. ID. No. 1053	ORF3519	2159468	2158452	tetrahydrodipicolinate succinylase	PIR:G70608	1,00E-72
SEQ. ID. No. 1054	ORF3522	2160865	2165046	helicase	TREMBL:BCX98455_2	1,00E-105

Table I (continued)

Seq.ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ.ID. No.1055	ORF3527	2166299	2166811	patch repair protein	PIRNEW:H81959	3,00E-34
SEQ.ID. No.1056	ORF3528	2168122	2168848	oxidoreductase	PIRNEW:T50594	3,00E-46
SEQ.ID. No.1057	ORF3530	2167994	2169214	aspartate aminotransferase	TREMBLNEW:AE004885_13	3,00E-78
SEQ.ID. No.1058	ORF3532	2169395	2170360	exopolyphosphatase	PIR:T36297	1,00E-80
SEQ.ID. No.1059	ORF3539	2173536	2175398	long chain fatty acid coA ligase	PIR:T35513	1,00E-129
SEQ.ID. No.1060	ORF3540	2176064	2175543	NAD(P)H oxidoreductase	PIR:B69977	2,00E-35
SEQ.ID. No.1061	ORF3542	2177910	2176543	exonuclease VII large subunit	PIR:B70898	4,00E-68
SEQ.ID. No.1062	ORF3545	2178378	2180783	anaerobic ribonucleotide	TREMBL:U73336_1	0
SEQ.ID. No.1063	ORF3546	2180853	2181659	anaerobic ribonucleotide reductase activase	TREMBL:U73336_2	6,00E-64
SEQ.ID. No.1064	ORF3548	2181890	2187025	(R)-hydroxyglutaryl-CoA dehydratase activator	PIR:F70325	2,00E-73
SEQ.ID. No.1065	ORF3556	2187334	2188467	gamma-glutamylcysteinyl synthetase precursor	TREMBL:AF128454_1	3,00E-33
SEQ.ID. No.1066	ORF3559	2189457	2191817	beta-glucosidase	TREMBL:BFAF6658_1	1,00E-116
SEQ.ID. No.1067	ORF3564	2192945	2194156	exo-1,3-beta-glucanase	TREMBLNEW:PB26160_1	3,00E-34
SEQ.ID. No.1068	ORF3567	2194826	2195982	beta-glucosidase	TREMBL:U92808_1	6,00E-54
SEQ.ID. No.1069	ORF3571	2197101	2199056	ABC transporter, ATP-binding protein	PIR:E72396	1,00E-104
SEQ.ID. No.1070	ORF3572	2199056	2201068	ABC transporter	TREMBLNEW:AP001509_253	1,00E-98
SEQ.ID. No.1071	ORF3573	2201251	2202273	transcriptional regulator LacI family	TREMBL:SCC57A_16	3,00E-43
SEQ.ID. No.1072	ORF3575	2202990	2203907	Glycosidase	PIR:JE0404	1,00E-73
SEQ.ID. No.1073	ORF3576	2204012	2205439	C4-dicarboxylate transporter	PIRNEW:G82431	8,00E-56
SEQ.ID. No.1074	ORF3579	2205668	2206633	carbohydrate kinase	TREMBL:SCC57A_19	8,00E-44
SEQ.ID. No.1075	ORF3581	2207166	2208170	transcription repressor of beta-galactosidase gene	TREMBLNEW:AP001514_24	2,00E-58
SEQ.ID. No.1076	ORF3582	2208838	2208239	beta-galactosidase	TREMBL:BLO242596_1	3,00E-62
SEQ.ID. No.1077	ORF3585	2210107	2208899	Aminotransferase	PIR:S32934	4,00E-54
SEQ.ID. No.1078	ORF3590	2210701	2214009	isoleucyl-tRNA synthetase	PIR:E70780	0
SEQ.ID. No.1079	ORF3592	2215780	2214854	Integrase	PIR:T13262	1,000-51

Table I (continued)

Seq. ID	Code	Start	Stop	Function	Best Blast Hit ID	E-val
SEQ. ID. No. 1080	ORF3591	2214208	2214855	type I site-specific deoxyribonuclease	PIR:S02167	7,00E-25
SEQ. ID. No. 1081	ORF3593	2216442	2215774	type I restriction-modification enzyme 2, S subunit	TREMBL:AF153410_1	1,00E-54
SEQ. ID. No. 1082	ORF3594	2216374	2217306	Mrr restriction endonuclease	PIR:D70657	2,00E-50
SEQ. ID. No. 1083	ORF3595	2217341	2219905	type I site-specific deoxyribonuclease	TREMBL:NEW:AF243383_16	1,00E-103
SEQ. ID. No. 1084	ORF3596	2219908	2221125	type I site-specific deoxyribonuclease	TREMBL:AF027167_1	1,00E-66
SEQ. ID. No. 1085	ORF3598	2222569	2225991	type I restriction enzyme R protein	TREMBL:AF013165_2	6,00E-93
SEQ. ID. No. 1086	ORF3602	2227282	2226065	methionine adenosyltransferase	TREMBL:NEW:CGL290443_2	1,00E-130
SEQ. ID. No. 1087	ORF3605	2228047	2229906	dihydroxy-acid dehydratase	PIR:T36294	0
SEQ. ID. No. 1088	ORF3607	2230986	2230003	methionyl-tRNA formyltransferase	PIR:C70901	2,00E-68
SEQ. ID. No. 1089	ORF3611	2234085	2231776	primosomal protein	PIR:G70900	5,00E-60
SEQ. ID. No. 1090	ORF3614	2234877	2234128	Phosphoserine phosphatase	PIR:T36772	3,00E-49
SEQ. ID. No. 1091	ORF3618	2234898	2235593	Unknown	PIR:S76640	1,00E-37
SEQ. ID. No. 1092	ORF3619	2235657	2237219	H ⁺ -transporting ATP synthase	PIR:F70512	1,00E-112
SEQ. ID. No. 1093	ORF3620	2237244	2238908	Unknown	PIR:C70512	9,00E-91
SEQ. ID. No. 1094	ORF3623	2240113	2241570	Unknown	TREMBL:MLCB2533_24	4,00E-88
SEQ. ID. No. 1095	ORF3626	2244677	2242119	Unknown	TREMBL:NEW:SC23B6_5	4,00E-49
SEQ. ID. No. 1096	ORF3630	2246254	2244812	adenylosuccinate lyase	PIR:NEW:A82237	1,00E-111
SEQ. ID. No. 1097	ORF3644	2255246	2254161	methanol dehydrogenase regulatory protein	TREMBL:NEW:AE004848_9	1,00E-64
SEQ. ID. No. 1098	ORF3646	2255918	2255280	uracil-DNA glycosylase	PIR:E70672	2,00E-77

[0028] The ORFs corresponding to SEQ. ID. NO. 2 to SEQ. ID. NO. 1098 nucleotide sequences are defined in table 1, supra, and are represented by their position in sequence SEQ. ID. No. 1. For example, the ORF3 sequence is defined by the nucleotide sequence between the nucleotides at position 785 and 2455 on the sequence SEQ. ID. No. 1, ends included.

[0029] The open reading frames have been identified via homology analyses as well as via analyses of potential ORF start sites. It is to be understood that each identified ORF of the invention comprises a nucleotide sequence that spans the contiguous nucleotide sequence from the codon immediately 3' to the stop codon of the preceding ORF and through the 5' codon to the next stop codon of SEQ. ID. No. 1 inframe to the ORF nucleotide sequence.

[0030] Table 1 also depicts the results of homology searches that compared the sequences of the polypeptides encoded by each of the ORFs to sequences present in public published databases. It is understood that in one embodiment, those polypeptides listed in Table 1 as exhibiting greater than about 99 % identity to a polypeptide present in a publicly disclosed database are not considered part of the present invention. Likewise in this embodiment, those nucleotide sequences encoding such polypeptides are not considered part of the invention.

[0031] As regards the homology with the ORF nucleotide sequences, the homologous sequences exhibiting a percentage identity with the bases of one of the ORF nucleotide sequences of at least 80%, preferably 90% and 95%, are preferred. Such homologous sequences are identified routinely via, for example, the algorithms described above and in the examples below. The said homologous sequences correspond to the homologous sequences as defined above and may comprise, for example, the sequences corresponding to the ORF sequences of a bacterium belonging to the Bifidobacterium family.

[0032] These homologous sequences may likewise correspond to variations linked to mutations within the same species or between species and may correspond in particular to truncations, substitutions, deletions and/or additions of at least one nucleotide. The said homologous sequences may also correspond to variations linked to the degeneracy of the genetic code or to a bias in the genetic code which is specific to the family, to the species or to the variant and which are likely to be present in Bifidobacterium.

[0033] According to a preferred embodiment the polynucleotide is a nucleotide sequence, which encodes the following polypeptides or fragments thereof:

(a) SEQ. ID. No.5 (ORF13)

MPTGRVRWFDAAKGYGFITSEEGKDVFLPAQALPTGVTTLRKGAKVEYSV
VDGRRGFPQAMDVRLIASAPSLVKATRPKADDMAAICEDLIKMLDAAGNTL
RRHRYPSAADSCKLATLLRAVADQFDVQD

(b) SEQ. ID. No.525 (ORF1827)

5 MTAAAQAPAPGKLEFKDDYTPDEAERVIRNSKGLPVGVRPKMVWTWKKA
 LLWAAIAIVCACGWAILAVSRGEQISAIWFLVVALSSYAIAYRFYAYYIQ
 IKIMRTDDANATPAERVHGDGANFERTDRRVLFQHFAGISGAGPLVGPIL
 10 AAQMGYLPSTLWIIILGVIFAGAVQDMLVLWISAKRRGRSLGQMATDEMKG
 FGGMILSIFLVVMTAIAMAFLALVAIKAMAASPAWVPSIGMTIPIALIMG
 CYQRFRLRPGRVIEETLLGFVLLVLDIVAGGWIASIPAVAAVFTLDAKQLV
 IALVIYSFAAAALPHWLLVTPRDYLSLTMKIGTLVLLVIGIIIANPSVKV
 PGLTELASTSTGPTFSGNLFPFLFITIACGALSGFHGAVSSGLTPKAVEK
 15 ENQIRMIGYGSMLVESFTAVIALIAAITISQGVYFSTNMSAAQITAASGV
 SISATSTPGEQADAAVKAVESMKVSDIEGNQMQVTWDSVDENGAAKTYEG
 AAALQAAADIGETSIVSRTGGATTTFAMGMANFLKSYLGGHDSMAFWYHF
 AIMFEALFILTTVDNGTRVARYQIGEMLGNVRKLKFKADPTWKPGN
 IITTLIATALWGGLLWVGVS DANGGINAMVPIFGISNQLLAAACFV
 20 LITVCVAKMGYWKHLWI PVVPLVWDIAVTFTADFKIFGPLSYFTT
 ASKYQAQIDSGELTGEALTNKAALSNAAYLDGVLSVFFLVMMGVFV
 VVGIVVVARTFAAGKYGAETTSEEPFVESQWFAPSSLVATALEKKV
 QREYSAKLHELVRNGQVAA

c) SEQ. ID. No.424 (ORF1473)

30 MTQSRRLVLRAVVEDYIRSQEPVGSTSLTRDHDLGVS SATIRNDMAALE
 DEGYLIQPHTSAGRVPTTEKGYRYFVDRLATVVPLSEAQRREGINSFLSGSV
 SLKDALQRSARLLSEITGQVAVVASPSLAKATLRHVEMVPVAMTTLLAVV
 ITDTGRVAQHGLTIASMPAVDEINRLSNTVNEQCDGLSLSKSAETVRSIA
 35 ASAGYESVRGVADTLADAFESMALDERANELYMSGTSHLAHSRSLADLAP
 LFDALQEEQVVLKMLMSNLSEETNASGVGVAIGSEMHTPGLLHASVSSGY
 GRSGAAGEPAGNDPVGEPETESETESQTNDEPIAFVGSIGPTHMDYAAT
 MAAVRAVARYLTAFLSEGRTQD

d) SEQ. ID. No.548 (ORF1905)

45 MYFKDGNDNAQRGGSTVRRSRQRRIMGRVVSYNEDVPRCTFCGKTEHQVR
 KLVAGPNASICDECIALCVDIISEERVKDAEVNSLSLPKPAQIFDYLNRY
 VIGQENAKRALSVAVYNHYKRVNMELQESAEQLDGNNHSGQTSKQAKQS
 VPTQTRATRRSNDPLADVEVAKSNILLGPTGVGKTYLAQALARVMNVPF
 50 VITDATTLEAGYVGDDVETVLQRLQLAADGDVSRQHGIIYIDEIDKIA
 RKSGENTSITRDVSGEGVQQALLKILEGTIASVPLEGTRKHKEQDVAQMD
 TRGILFICGGAFFVGLTDIVRKRLGRRETGFGANWHDADMKDEELLEQVNA
 DDLAEFGLLPEFIGRLPVTSVLKELTVDDLTAILTQPANALIKQYRKLFA
 VDGVDLQFTEQAIRAIADIAIKQGTGARGLRSI IERTLQDTMFQLPSLDD
 55 VRQVIVDKASVEGSSTPKLLREAVDVPQGRLLKVAQSVLLDRVRTHEA

e) SEQ. ID. No.74 (ORF219)

5 MSEQLMEQYRLRGQRKCRNACIAAIVTVVLVLAVAGGVWWTAGDGSALVR
 NMFKPKATPATQPVVNSTATFAYRTAPEFLAMEAGDRGTGNVNYSPASMW
 MALAIAAQGANGTTRSQNLNELLGSGSLTDSYQSLSSINGQYSGAKSEM
 10 SAANSLWIDDDYSLASDYQSTVKKMFEEVTTLPFDDQAAAKMSDWIAKH
 TNGSLKPKITLRDREVLSIINTVYADGRWKDPFEEQSTGNGTFHGEAGDA
 QVPMMHQTFSQMAYGHDEYNTWQORVEIPFDNGGNLAIIVLPAEGHFDELAG
 DAEKLSWAFGTCSTASLGEGAMGCAADSMPGWGVSVNSVMVNVTLPRFTI
 DSMFDSEATIKAFEKLGVTDAFSAGDADFTKMIDTGSNGENLYIGSILQG
 15 TRIEVNEAGAKAMSFTKVGADSVSAPVDNVEFTVDRPFLYSYVTPDGIPL
 FIGAVRNLGGVGGEN

f) SEQ. ID. No.576 (ORF1972)

20 MQIRPGSMYPLGASYDGAGVNFALYSQVAQKVELCLFDEHDVETRIEMTE
 RNSYVWHNYIPGLHPGQRYGYRVYGPYDPVHGLRCNPNKLLLDPYAKAIE
 25 GNIDGDESLFSYWFKSPDDNSAMNDLDSAAHTMKSAVINPYFDWGNDQHP
 YISYHDSVIYEAHVRGMTNLNMDVPPDIRGTIYAGLAYPSVIEYLKKGIT
 AIELMPIHQFVNDSTFLQEKGLSNYWGYNITIGFFAPHNAYSSSGERGEQVN
 EFKSMVKAYHRAGMEVILDVVYNHTAEGNHMGPTLSFKGIDNASYYRLVE
 30 GDQOHYFDTTGTGNSLLMRSPHALQLITDSLRYWVTEMHVDGFRFDLAAT
 LARQFQEVDKLSAFFDIVEQDPIISRVKLIAPWDLGSGGYQVGGFPSSW
 SEWNGRYRDTVRDFWRSQPSTLPEFASRLMGSSDLYQVNGRRPVASVNF

35 TAHDGFTMNDLVSYNEKHNEANGEGRDGESENRSWNCGVEGPTNIPDVN
 DLRQRQMRNMFATLLFSQGI PMICGGDEVARTQOGNNNAYCQDNEISWTN
 WHLDKGRKELLAFVSKLIHLRLDHPVLHRRRFFFTGREPGDDSENTIPQVEW
 40 FDHTGSIMDMDDWQNTAFSMMIYLNGSDIPEVDWYGNRMVDNDFILIFN
 AHYEPIMFTLPDERYGRKWQLVVDTHNPNEPALSYEAGFMITAQSRSLM
 LMSAKKPKKPMGL

g) SEQ. ID. No.403 (ORF1403)

45 MEIRARPHMASGSYRELFSAARMYGMQYIQQTIVGIDGSEARFFGYVADN
 SEEMEPDRIRPAILILPGGGYAMTSDREAEPVALQFLAKGFAVFVLRYSV
 50 QPSRYPVALLEAAEAMRLIRANVDQWHVNPAQVAVLGFSAGGHAAANLAT
 SVGDEDIREQGGMDPDVAVRNALMLSYPVITAGKYAHRGSFQCLLGDOAH
 NQALLDKFSIEKHIDAKTPPVFVWHTMTDDAVPVENTLMLIQACRAAGVS
 IEAHLFPEGSHGLSLANAETAGNGFYAHIVECVQCWPDLAEAWLRRLE

(h) SEQ. ID. No.804 (ORF2676)

5 MFLKPEQQLERCRRIVRQRVDPHIHPSIAQLTVESYDIPGEPMPSPDEFFA
 KLDRGDIDFKPFMLGSEWGTTWGTWVFRLTGTVPAGYPKGKPLELILDLG
 WYPHSCGGHIEGLVYRADGTAIKAVHPLNYWVPFMDAEGNAQVPVAEDGS
 10 FTLYLEAASNPLLLGVPPFIETELGDHATGKPDEPYVFKSADLAEFDERY
 ENYSVDLDVSSLMFEADKQSPRYWQLAKALQRS LNAYDERNPESVEAAR
 AVLAGVLAKPANASAMNVSAIGHAHIDS AWLWPVRETRRKVARTVSNALA
 LMDADPDFKYAMSSAQQYAWLEEDHPDIFKRMKRRIEGRFIPVGGMWVE
 ADGMLPAGESLIRQIAYGRKYFKEHLGVEPKGVWLPDSFGYTGAWPQIAR
 15 RAGYEWFLTQKISWNDTTKFPHHSEFMWEGIDGSRI FTHFPADTYAAWCK
 VQELDYAEKNFQDKDLSDRSLLLFGFGDGGGGPTRNMMEHLHRYENLEGV
 SKVSIIEPNDFDKAHQQLAENAGPEMPVWKGELEYELHRGTLTSQQDMK
 RGCQREESLLRTVEYLGAAAVLSDPEYVYPREELDRIWKTLLLNQFHDIL
 PGSAIAWVHREAREDYRRDLKRLAEIAQDMCAVLRKANPQADLLAEARIS
 20 QFRNDGASWHANRINEPTDALS VLTQTLDNGRVLLANGVLSVTIEADGTI
 SSLLDEEHGRELVPACTRLGQYELLRDEPAVWDAWEIERESLLMANAVTG
 SIESVNTENGAAQVHVHTADGDTVITTTITLTPGSHTLDFHADIDWHERE
 RFLKVDLPLGIVADQATYDCQYGLIRRP IVKNTASDEAKYESSTNRFAII
 GDAGYAAAVINGSVYGS DASPIAGNAAEGRDSGTMFRLSLLSAPTFPDPR
 25 TDIGSHEFDWSV VADATVDRALDAAGVLNAPVLHDVPDITPLASIESVNG
 TVVLDWMKLADGSGDLIVRAYEAAAGGQADAMLHVC PALAGASVHETNVL
 EGDDLAADLPVALQDGRQNAEGATLHFGPFQLATLRITR

(i) SEQ. ID. No.313 (ORF1077)

35 MISRDGWAVIDDSAANII IETDTVNGKANPFGTWVSPRATAETDLYFFGY
 GHRYIEAVRDFYRLTGPTLLPRFAMGNWWSRYRYRTQDGYLALMDRFRK
 EGIPFTTSVIDMDWHRVDDVDPKYGSGWTGYSWNRELFPDPPAFLADLHR
 RGLRTTLNVHPRDGVRAFEDAYPEVAKRVGIDPATEENVEFDLTNPDFVD
 40 AYFDMHHRMEAEGVDFWWLDWQQGGVTRQKGLDPLWMLNHHMYLDSGRGG

45 NWPLTFSRYAGPGSHRYPVGFSGDTIVTWESLAFQPQFTATASNIGYGWW
 SHDIGGHMFGYRNEELEARWYQLGAFSPINRLHSSNSPFGSKEPWNFNRD
 VSAAMVDALRLRHAMPYLYTMNYRAAEAGRPLVEPMYWQNPDPDAYEV
 PDEFRTGTELVVAPIVSPDDAAACRGRADAWLPQGEWFDFFDGRRYVSSD
 AAGRRLLEVWRS LDRTPVFAKAGAI VPLQDVAESGEA INSIANPQALRVLV
 50 FPGADGSFVMREDRGTWGAPSADTAIAFTWGGADASPSAFTVAPVTGDT
 AVPELRDWTVVFRGVAPVDAASGVRAWSGEAPVEATVAYDEATMSLT VSV
 TGISSAASLRIEIPGGLRIADNPVESDAMDLLLHAQMLYRTKELALQAVH
 KLGIGAIGALRTMNRGPRYANDFWITDMPDAVAGALEEILLRS

55 [0034] According to another preferred embodiment the present invention comprises a polynucleotide encoding a fusion protein, comprising any one of SEQ. ID. NO. 2 to SEQ. ID. NO. 1098 ligated in frame to a polynucleotide encoding a heterologous polypeptide. The skilled person is well acquainted with techniques performing such a ligation and expressing the corresponding fusion-polypeptide in an appropriate cell.

[0035] The present invention also relates to recombinant vectors for the cloning and/or the expression of a nucleotide sequence according to the present invention. The vectors comprise elements necessary to enable expression and/or secretion of the nucleotide sequences in a given host cell, such as a promoter, signals for initiation and for termination of translation, as well as appropriate regions for regulation of transcription. For example, expression of a protein or peptide may be controlled by any promoter/enhancer element known in the art. Exemplary promoters are the CMV promoter, the SV40 early promoter region, the promoter contained in the 3' long terminal repeat of the rous sarcoma virus, the herpes thymidine kinase promoter, the regulatory sequences of the metallothionein gene, or, for prokaryotic expression systems, the β -lactamase promoter, the tac promoter or the T7 promoter.

[0036] The vector should be capable of being stably maintained in the host cell and may optionally possess particular signals specifying the secretion of the translated protein. These different elements are chosen according to the host cell utilized. To this effect the nucleotide sequences according to the invention may be inserted into autonomously-replicating vectors within the chosen host, or integrative vectors in the chosen host, such as e.g. yeast artificial chromosomes, plasmids or viral vectors. It will be appreciated that the vector may well be the plasmid according to SEQ. ID. No. 1099 or a recombinant form thereof, which has been supplemented by particular ori's that enable a high copy number.

[0037] Any of the standard methods known to those skilled in the art for inserting DNA fragments into a vector may be used to construct expression vectors containing a chimeric gene consisting of appropriate transcriptional/translational control signals and the protein coding sequences. These methods may include in vitro recombinant DNA and synthetic techniques and in vivo recombinants (genetic recombination).

[0038] The vector may be used for transcription and/or translation of a nucleic acid comprised by SEQ. ID. NO. 1 to produce RNA or antisense RNA, respectively. Such a vector can remain episomal or become chromosomally integrated, as long as it can be transcribed to produce the desired transcript.

[0039] The antisense nucleic acids of the invention comprise a sequence complementary to at least a portion of a RNA transcript of a polynucleotide sequence in SEQ. ID. No. 1, designating a sequence having sufficient complementarity to be able to hybridize with the RNA, forming a stable duplex. In the case of double-stranded antisense nucleic acid sequence, a single strand of the duplex DNA may thus be tested, or triplex formation may be assayed.

[0040] The invention also encompasses host cells transformed with a nucleic acid or a vector according to the present invention and as described above. These cells may be obtained by introducing into an appropriate cell a nucleotide sequence or a vector as defined above, and then culturing the said cell under conditions allowing the replication and/or the expression of the transformed/transfected nucleotide sequence.

[0041] The host cell may be chosen from eukaryotic or prokaryotic system, such as for example bacterial cells, yeast cells, animal cells as well as plant cells. In the context of this invention a cell shall be understood to comprise higher biological systems. Such as animals, whole plants or parts thereof. Furthermore, a host cell strain may be chosen which modulates the expression of the inserted sequences, or modifies end processes the gene product in the specific fashion desired.

[0042] A preferred host cell for the expression of the proteins of the invention consists of prokaryotic cells, such as gram negative or gram positive bacteria. A further preferred host cell according to the invention is a bacterium belonging to the Bifidobacterium family, more preferably belonging to the species Bifidobacterium longum or chosen from a microorganism associated with the species Bifidobacterium longum.

[0043] The transformed/transfected cells according to the invention may advantageously serve as a model and may be used in methods for studying, identifying and/or selecting compounds capable of being responsible for any of the beneficial effects brought about by the present Bifidobacterium strain.

[0044] The invention further provides polypeptides encoded by the Bifidobacterium longum ORFs, in particular those listed in table 1 and identified in the sequence listings. In the present description, the terms polypeptide, peptide and protein are used interchangeably. Furthermore the present invention also pertains to method for preparing such polypeptides by recombinant means comprising the steps of (a) culturing a host cell according to the present invention under conditions suitable to produce the polypeptide encoded by the polynucleotide; and (b) recovering the polypeptide from the culture.

[0045] It will be appreciated that the above polypeptides may also be obtained using combinatory chemistry, wherein the polypeptide is modified at some locations before testing them in model systems, so as to select the compounds which are the most active or which exhibit the desired properties.

[0046] In this context, chemical synthesis has the advantage of being able to use non-natural amino acids or non-peptide bonds. Accordingly, in order to e.g. extend the life of the polypeptides according to the invention, it may be advantageous to use such non-natural amino acids, for example in the D form, or alternatively amino acid analogues, preferably sulphur-containing forms.

[0047] Finally, the structure of the polypeptides according to the invention, its homologous or modified forms, as well as the corresponding fragments may be integrated into chemical structures of the polypeptide type and the like. Accordingly, in order to preserve the polypeptide in an in vivo environment it will be preferred to provide at the N- and C-

terminal ends compounds which convey a resistance to degradation to proteases.

[0048] It will also be appreciated that the different polypeptides according to the present invention and produced by the above method may represent antigens to the immune system of a host animal, so that antibodies may be produced directed against said polypeptides. These antibodies may be used for the detection of a polypeptide of interest in a mixture or generically of a strain of *Bifidobacterium* in a sample. In addition they may be used as research tools by e.g. producing antibodies against cellular surface epitopes and determining the effect of blocking certain polypeptides on the bacterial cell wall. Therefore, according to another aspect, the invention provides antibodies directed to epitopes on the various polypeptides provided by this invention.

[0049] According to another aspect the present invention also provides a method for the detection and/or identification of *Bifidobacterium longum* in a biological sample. This method may comprise several techniques known in the art, such as PCR or simply hybridisation with a suitable probe. Alternatively, an antibody raised against a cell wall epitope of *Bifidobacterium longum* may be used for said purpose. It will be appreciated that the above method may also be reversed and the presence of antibodies against *Bifidobacterium* may be determined by contacting the sample to be tested with a polypeptide of *Bifidobacterium* under conditions to allow formation of immune complexes.

[0050] The polypeptides according to the invention, the antibodies according to the invention described below and the nucleotide sequences according to the invention may be used in *in vitro* and/or *in vivo* methods for the detection and/or the identification of bacteria belonging to the species *Bifidobacterium* in a biological sample (biological tissue or fluid) which is likely to contain them. These methods, depending on the specificity of the polypeptides, of the antibodies and of the nucleotide sequences according to the invention which will be used, may detect and/or identify the bacterial variants belonging to the species *Bifidobacterium* as well as associated microorganisms capable of being detected by the polypeptides, the antibodies and the nucleotide sequences according to the invention which will be chosen. It may, for example, be advantageous to choose a polypeptide, an antibody or a nucleotide sequence according to the invention, which is capable of detecting any bacterium of the *Bifidobacterium* family by choosing a polypeptide, an antibody and/or a nucleotide sequence according to the invention which is specific to the family.

[0051] All the sequences referred to herein (SEQ ID. NO. 1 to SEQ ID. NO. 1099) are listed in the attached sequence listings which is to be considered as part of the specification.

[0052] The invention also comprises the nucleotide sequences or polypeptides according to the invention covalently or noncovalently immobilized on a solid support. In the first case such a support may serve to capture, through specific hybridization, the target nucleic acid obtained from a biological sample to be tested. If necessary, the solid support is separated from the sample and the hybridization complex formed between the capture probe and the target nucleic acid is then detected by means of a second probe, called detection probe, labelled with an easily detectable element.

[0053] Such support may take the form of so-called DNA array or DNA chips, a multitude of molecular probes precisely organized or arrayed on a solid support, which will allow sequencing genes, studies of mutations contained therein and the expression of genes, and which are currently of interest given their very small size and their high capacity in terms of number of analyses.

[0054] The function of these arrays/chips is based on molecular probes, mainly oligonucleotides which are attached to a carrier having a size of generally a few square centimetres or more as desired. For an analysis the carrier (DNA array/chip) is coated with probes that are arranged at a predetermined location of the carrier. A sample containing fragments of a target nucleic acid to be analysed, for example DNA or RNA or cDNA, that has been labelled beforehand, is subsequently contacted with the DNA array/chip leading to the formation, through hybridization, of a duplex. After a washing step, analysis of the surface of the chip allows the effective hybridizations to be located by means of the signals emitted by the labels tagging the target. A hybridization fingerprint results from this analysis which, by appropriate computer processing, allows to retrieve information such as the expression of genes, the presence of specific fragments in the sample, the determination of sequences and the presence of mutations.

[0055] The hybridization between the probes of the invention, deposited or synthesized *in situ* on the DNA chips, and the sample to be analysed, may, e.g. be determined by means of fluorescence, radioactivity or by electronic detection.

[0056] The nucleotide sequences according to the invention may be used in DNA arrays/chips to carry out analyses of the expression of the *Bifidobacterium* genes. This analysis is based on DNA arrays/chips on which probes, chosen for their specificity to characterize a given gene, are present. The target sequences to be analysed are labelled before being hybridized onto the chip. After washing the labelled compounds are detected and quantified, with the hybridizations being carried out at least in duplicate. Comparative analyses of the signal intensities obtained with respect to the same probe for different samples and/or for different probes with the same sample, determine a differential transcription of RNA derived from the sample.

[0057] The DNA arrays/chips according to the present invention may also contain nucleotide probes specific for other microorganisms, which will enable a serial testing allowing rapid identification of the presence of a microorganism in a sample.

[0058] The principle of the DNA chip, as detailed above may also be used to produce protein chips on which the

support has been coated with a polypeptide or an antibody according to the invention, or arrays thereof, in place of the DNA. These protein chips make it possible to analyse the biomolecular interactions (BIA) induced by the affinity capture of target analytes onto a support coated e.g. with proteins, by surface plasma resonance (SPR). The polypeptides or antibodies according to the invention, capable of specifically binding antibodies or polypeptides derived from the sample to be analysed, may thus be used in protein chips for the detection and/or the identification of proteins in samples.

[0059] The present invention also relates to a computer readable medium having recorded thereon one or more nucleotide and/or a polypeptide sequences according to the invention. This medium may also comprise additional information extracted from the present invention, such as e.g. analogies with already known sequences and/or information relating to the nucleotide and/or polypeptide sequences of other microorganisms so as to facilitate the comparative analysis and the exploitation of the results obtained. Preferred media are e.g. magnetic, optical, electrical and hybrid media such as, for example, floppy disks, CD-ROMs or recording cassettes.

[0060] The invention also relates to kits or sets for the detection and/or the identification of bacteria belonging to the species *Bifidobacterium longum* or to associated microorganisms, which comprises, a polypeptide according to the invention, where appropriate, the reagents for constituting the medium appropriate for the immunological or specific reaction, the reagents allowing the detection of the antigen-antibody complexes produced by the immunological reaction between the polypeptide (s) of the invention and the antibodies which may be present in the biological sample, it being possible for these reagents also to carry a label, or to be capable of being recognized in turn by a labelled reagent, more particularly in the case where the polypeptide according to the invention is not labelled, a reference biological sample (negative control) free of antibodies recognized by a polypeptide according to the invention, a reference biological sample (positive control) containing a predetermined quantity of antibodies recognized by a polypeptide according to the invention.

[0061] The invention also relates to a kit or set for the detection and/or the identification of bacteria belonging to the species *Bifidobacterium longum* or to an associated microorganism, or for the detection and/or the identification of a microorganism, wherein the kit comprises a protein chip according to the invention.

[0062] The present invention also pertains to a novel microorganism termed NCC2705, which has been deposited according to the Budapest Treaty with the Institute Pasteur on January 29th, 2001 and received the deposit no. CNCM I-2618. This micro-organism belongs to the genus *Bifidobacterium*, species *Bifidobacterium longum* and is a probiotic micro-organism, i.e. it may pass the gastro-intestinal tract in an essentially live and viable form and has the capability of preventing colonization of the intestine with pathogenic bacteria causing diarrhea and in addition may prevent or reduce the occurrence of infection of intestinal cells by rotaviruses.

[0063] The microorganism is gram positive, catalase negative and CO₂ production negative; it produces L(+) lactic acid and essentially prevents colonization of intestinal cells by bacteria bringing about diarrhea, such as pathogenic *E. coli*, e.g. enteropathogenic *E. coli* (EPEC), or salmonella, e.g. *Salmonella typhimurium* and prevents infection of intestinal cells by rotaviruses.

[0064] The novel microorganism may be used for the preparation of a variety of carrier materials, such as e.g. milk, yogurt, curd, fermented milks, milk based fermented products, fermented cereal based products, milk based powders, infant formulae and may be included in the support in an amount of from about 10⁵ cfu / g to about 10¹¹ cfu / g. For the purpose of the present invention the abbreviation cfu shall designate a "colony forming unit" that is defined as number of bacterial cells as revealed by microbiological counts on agar plates.

[0065] The present invention also provides a food or a pharmaceutical composition containing at least the *Bifidobacterium* NCC 2705 and/or containing a supernatant, in which the microorganisms have been grown or an active fraction/metabolite thereof, respectively.

[0066] For preparing a food composition according to the present invention at least one of the *Bifidobacteria* of the present invention is incorporated in a suitable support, in an amount of from about 10⁵ cfu / g to about 10¹² cfu / g, preferably from about 10⁶ cfu / g to about 10¹⁰ cfu / g, more preferably from about 10⁷ cfu / g to about 10⁹ cfu / g.

[0067] In case of a pharmaceutical preparation the product may be prepared in form of tablets, liquid bacterial suspensions, dried oral supplements, wet oral supplements, dry tube feeding or a wet tube feeding with the amount of the *Bifidobacterium*/*Bifidobacteria* to be incorporated therein being in the range of up to about 10¹² cfu / g, preferably from about 10⁷ cfu / g to about 10¹¹ cfu / g, more preferably from about 10⁷ cfu / g to about 10¹⁰ cfu / g.

[0068] The activity of the novel microorganism in the individual's intestine is of course dose dependent. That is, the more the novel microorganism or an active component thereof is incorporated by means of ingesting the above food material or the pharmaceutical composition the higher the protective and/or curing activity. Since the novel microorganism is not detrimental to mankind and animals and has eventually been isolated from baby feces a high amount thereof may be incorporated so that essentially a high proportion of the individual's intestine will be colonized by the novel microorganisms.

[0069] Yet, according to another preferred embodiment the supernatant of a culture of the *Bifidobacterium* of the present invention, or an active fraction thereof, may be used for preparing the carrier. The supernatant may be used

as such or may be dried under conditions that do not destroy the metabolic compounds secreted by the microorganisms into the liquid medium, such as e.g. freeze drying, and may be included in the carrier. In order to minimize the number of unknown compounds in the supernatant the Bifidobacteria will preferably be grown in a defined media, the composition of which is known and does not negatively affect the host incorporating it. Further, the skilled person will, based on his general knowledge optionally deplete the supernatant from unwanted products, such as e.g. by means of chromatography.

[0070] The present inventors have investigated baby feces and isolated a variety of different bacterial strains therefrom. These strains were subsequently examined for their capability to prevent prevent colonization and/or invasion of epithelial cells with bacteria that are known to cause diarrhea, such as E.coli, Sigella, Klebsiella, Yersinia, Pseudomonas aeruginosa, Listeria, Streptococcus, Staphilococcus, Clostridium difficile, H. pylori and also Candida albicans.

[0071] Several bacterial genera comprising Bifidobacterium, Lactococcus and Streptococcus were screened for their diarrhea inhibitory properties. The tests for the inhibitory property were performed with pathogenic microorganisms, such as E.coli, Klebsiella, Yersinia, Pseudomonas aeruginosa, H. pylori, and Salmonella typhimurium as representatives for pathogenic micro-organisms causing diarrhea in affected individuals.

[0072] The various bacteria were grown in a suitable medium, such as MRS, Hugo-Jago or M17 medium at temperatures of from about 30 to 40°C corresponding to their optimal growth temperature. After reaching stationary growth the bacteria were collected by centrifugation and resuspended in physiological NaCl solution. Between the different tests the bacterial cells were stored frozen (-20°C).

[0073] For assessing anti-bacterial properties the following approaches were chosen.

[0074] According to one protocol the cultured Bifidobacterium of the present invention was examined for its capability to decrease the viability of the different pathogenic micro-organisms. To this end, a culture of pathogenic bacteria was contacted with a concentrated supernatant of a Bifidobacterium culture and the growth potential of the pathogenic bacteria was assessed.

[0075] According to a second protocol the adhesion capability of the Bifidobacteria of the present invention to T₈₄ cells, a cell culture model for the intestine, was determined by culturing the Bifidobacterium with T₈₄ cells and the rate of adhesion was assessed.

[0076] According to another protocol the potential of the Bifidobacterium of the present invention to prevent infection of intestinal cells by Salmonella, using the cell line Caco-2 as a model for the intestine, was determined. In this respect, the supernatant of a cell culture of the Bifidobacteria of the present invention was added together with the pathogenic microorganism to the intestinal cells and the rate of adhesion, or invasion, respectively, was assessed.

[0077] Thus, it could be shown that the cultured Bifidobacterium and the supernatant proved to be extremely effective in preventing both adhesion to and invasion into the intestinal cells indicating that one or more metabolic compounds secreted by the microorganism is/are likely to be responsible for the anti-diarrhea activity.

[0078] According to yet another protocol it was further assessed, whether NCC2705 would be capable to prevent invasion of epithelial cells by rotaviruses. Two different protocols were applied. According to one protocol the various bacterial strains were examined for their direct interaction with the rotavirus strain while in the second protocol the bacteria were screened for those strains that interact with cellular rotavirus receptors.

[0079] The first protocol involved contacting the respective bacterial suspension each with a different rotavirus strain and incubating in suitable media. Subsequently, the virus-bacteria mixture was applied to a monolayer of cells of the human undifferentiated colon adenoma cells HT-29 (intestinal epithelial cell line) and incubation was continued. Virus replication was then assayed.

[0080] The second protocol involved incubating the respective bacterial suspension first together with a monolayer of cells of the human undifferentiated colon adenoma cells HT-29 and adding the virus subsequently. After continued incubation virus replication was assayed.

[0081] Rotavirus replication was assessed by histo-immunological staining of rotavirus proteins in infected cells. A rotavirus inhibitory effect was attributed to a given bacterium when the number of infected cells was reduced by 90% in the cell culture inoculated with rotavirus plus the indicated bacteria in comparison with cells inoculated only with rotavirus.

[0082] The present invention will now be described by way of examples without limiting the same thereto.

[0083] Media and solutions:

MRS (Difco)

Hugo-Jago (tryptone 30g / 1(Difco), yeast extract 10 g / 1(Difco), lactose 5 g / 1 (Difco), KH₂PO₄ 6 g / 1, beef extract 2 g / 1(Difco), agar 2 g / 1(Difco))

M17 (Difco)

Eugon Tomato Agar (Canned tomato juice 400 ml, Eugon agar BBL 45.5 g, Maltose Difco 10 g, HemIn Sigma 5mg, Agar Difco 5 g, distilled water 600 ml)

DMEM (Dulbecco's modified Eagle medium)

EP 1 227 152 A1

CFA (according to Ghosh et al. Journal of Clinical Microbiology, 1993 31 2163-6)

Müller Hinton agar (Oxoid)

LB (Luria Bertani, Maniatis, A Laboratory Handbook, Cold Spring Harbor, 1992)

C¹⁴-acetate (53,4 Ci/mMol, Amersham International PLC)

PBS (NaCl 8g/l, KCl 0.2 g/l, Na₂HPO₄ 1.15 g/l, KH₂PO₄ 0.2 g/l)

Trypsin-EDTA solution (Seromed)

FCS Fetal calf serum (Gibco)

[0084] *E. coli* DAEC C 1845 was obtained from Washington University, Seattle and *E. coli* JPN15 was obtained from the Center for Vaccine Development of the University of Maryland, USA). The *Salmonella typhimurium* strain SL1344 was obtained from the department of Microbiology, Stanford University, CA, USA. This strain acts as a pathogen on mice and is resistant to Streptomycin. It adheres to Caco-2 colon cells (Finlay and Falkow, 1990). The *Klebsiella* was obtained from stock clinical isolates from the microbiological laboratory of the Faculté de Pharmacie Paris XI, Châtenay-Malabry, France. The *Yersinia* was obtained from INSERM Unit 411, Hôpital Necker, Paris, France. The *Pseudomonas aeruginosa* was obtained from stock clinical isolates from the microbiological laboratory of the Faculté de Pharmacie Paris XI, Châtenay-Malabry, France.

[0085] The *H. pylori* was obtained from Institute of Microbiology, Lausanne University, Lausanne, Switzerland.

[0086] Human rotavirus Wa (G1 serotype) and simian rotavirus SA-11 (G3 serotype) were obtained from P.A. Offit, Children's Hospital of Philadelphia, U.S.A. The DS-IxRRV reassortant virus was obtained from A. Kapikian, NIH Bethesda, U.S.A. The serotype 4 human rotavirus Hoch1 was obtained from P. Bachmann, University of Munich, Germany.

Example 1

Isolation of Bifidobacteria

[0087] Fresh feces were harvested from diapers of 16 healthy babies 15 to 27 days old. 1 g of fresh feces was placed under anaerobic conditions for transportation to the laboratory and microbiological analyses were run within 2 hours from sampling by serial dilutions in Ringer solution and plating on selective media. Eugon Tomato Agar (Canned tomato juice 400 ml, Eugon agar BBL 45.5 g, Maltose Difco 10 g, Hemin Sigma 5mg, Agar Difco 5 g, distilled water 600 ml) incubated anaerobically at 37°C for 48 hours was used to isolate bifidobacteria. Colonies were randomly picked up and purified. Physiological and genetic characterisation was performed on the isolates.

Example 2

Cultivating cell lines

Caco-2 cells:

[0088] For the inhibition assays the cell line Caco-2 was utilized as a model of mature enterocytes of the small intestine. This cell line presents characteristic of intestinal cells such as e.g. polarization, expression of intestinal enzymes, production of particular structural polypeptides etc.. The cells were grown on different supports, namely on plastic dishes (25 cm², Corning) for growth and propagation, on defatted and sterilized 6 well glass plates (22 x 22 mm, Corning) for the adhesion and the inhibition tests. After the second day in culture the medium (DMEM) was changed on a daily basis. Before use the medium was supplemented with 100 U/ml penicilline/streptomycine, 1 µg/ml amphotericine, 20 % FCS inactivated at 56 °C for 30 min and 1 % of a solution containing non-essential amino acids (10 mM) (Eurobio, Paris, France). Culturing was performed at 37 °C in an atmosphere comprising 90% air and 10% CO₂. The cells were splitted every six days. The cells were detached from the walls of the well by treatment in PBS with 0.015 % trypsin and 3 mM EDTA at pH 7.2. For neutralizing the effect of trypsin an equal volume of the culture medium containing FCS was added to the cell suspension obtained, the mixture was centrifuged (10 min at 1000 rpm) and the pellet was again dissolved in culture medium. Living cells (not dyed with trypan blue) were counted. About 3.5 x 10⁵ living cells were transferred to a new culture bottle and about 1.4 x 10⁵ cells per well and cultivated until a confluent monolayer was obtained.

T₈₄ cells:

[0089] For the adhesion assays the cell line T₈₄ was utilized as a model of colon cells from the intestine. This cell line presents characteristics of intestinal cells such as e.g. polarisation, expression of intestinal enzymes, production of particular structural polypeptides etc.. T₈₄ cells were obtained from University of California, San Diego, CA. Cells

were grown in DMEM (50%) and Ham's F12 (50%) supplemented with 2 mM glutamine, 50 mM HEPES, 1% non-essential amino acids and 10% inactivated (30 min, 56°C) fetal calf serum (Boehringer, Mannheim, Germany) at 37°C in a 10% CO₂/90% air atmosphere. Cells were seeded at a concentration of 10⁶ cells per cm². Cells were used for adherence assays at late post-confluence, i.e., after 10 days.

[0090] All strains except Bifidobacteria were kept at -80°C in their culture medium containing 15% glycerol. As the number of transfers into new media has an influence on the adhesion factors, the Salmonella strain was only transferred twice within a period of 24 hours, the first transfer taking place when the strain was frozen. All cultures were raised aerobically.

Bifidobacteria

[0091] The bacterial strain (*Bifidobacterium longum* CNCM I-2618 (NCC2705) was stored at -20 °C in MRS medium containing 15 % glycerol. The strain was grown under anaerobic conditions in MRS and transferred twice to new media at intervals of 24 hours before use in the inhibition assays. For the assay a concentration of 2 x 10⁹ cfu/ml was utilized. The supernatant was collected by centrifugation for 1 hour at 20.000 rpm and the supernatant obtained was subsequently checked for the presence of bacteria. The strains of *Bifidobacterium* were cultivated anaerobically in MRS during 18 hours at 37°C. The cultures were then centrifuged (20 min. at 4°C), the supernatant was collected, lyophilized, returned to the solution and then concentrated ten times (10x). The pH of the supernatant was finally adjusted to 4.5.

E. coli C 1845:

[0092] The first passage after thawing was effected on a CFA - Müller Hinton agar, which is suitable to effect expression of adhesion factors by the bacterium. Before each experiment the bacterial cells were incubated at 37 °C with a transfer to a new medium being effected twice after 24 hours each.

Klebsiella:

[0093] Bacteria were grown overnight for 18 hrs at 37°C in Luria broth.

Yersinia:

[0094] Bacteria were grown overnight for 18 hrs at 37°C in Luria broth.

Pseudomonas aeruginosa:

[0095] Bacteria were grown overnight for 18 hrs at 37°C in Luria broth.

H. pylori:

[0096] Bacteria were grown on Brain-Heart Infusion (BHI)-agar plates containing 0.25% yeast extract (Difco Laboratories, Detroit, MI), 10% horse serum and 0.4% Campylobacter selective complement (Skirrow supplement, SR 69 ; Oxoid Ltd, Basingstoke, England).

Example 4

[0097] The Caco-2 and T₈₄ monolayers, prepared on glass coverslips which were placed in six-well Corning tissue culture plates (Corning Glass Works, Corning, NY), were washed twice with phosphate-buffered saline (PBS). Bifidobacteria (1 ml, 4x10⁸ bacteria/ml in spent culture supernatant, treated-supernatant or fresh MRS broth) were added to 1 ml of the cell line culture medium. This suspension (2 ml) was added to each well of the tissue culture plate and the plate incubated at 37 °C in 10% CO₂/90% air. After 1 hour of incubation, the monolayers were washed five times with sterile PBS, fixed with methanol, stained with Gram stain, and examined microscopically. Each adherence assay was conducted in duplicate over three successive passages of intestinal cells. For each monolayer on a glass coverslip, the number of adherent bacteria was evaluated in 20 random microscopic areas. Adhesion was evaluated by two different technicians to eliminate bias.

[0098] The results are shown in Fig. 1 from which it becomes obvious that NCC2705 is capable to adhere to intestinal cells as compared to the known cell line GG (WO 97/00078), Lal (EP 0 577 903) or another Bifido strain (BL28/Cal).

Example 5

[0099] As candidates for pathogenic bacteria *E.coli*, *Klebsiella*, *Yersinia*, *Pseudomonas aeruginosa* and *H. pylori* were used.

[0100] Based on a culture of NCC2705 kept in MRS medium for 18 hours, an exponentially growing culture was produced (3 hours at 37°C). 2 ml of this solution were removed and centrifuged for 5 min. at 5500 g, +4 °C. After collection of the supernatant the cell pellet was washed in sterile PBS. After centrifuging, the pellet was collected and 2 ml of sterile PBS were added. The bacteria were counted and the suspension was adapted in such a way that between 1 and 5 x 10⁶ bacteria / ml were produced.

[0101] The assessment of the antimicrobial effect exerted by the *Bifidobacteria* of the present invention was carried out according to the Lehrer method described in Lehrer et al., J. Immunol. Methods 137 (1991), 167-173, which document is incorporated here by way of reference. The results thereof are shown in Fig. 2 and 3.

[0102] From the above results it may be seen that the *Bifidobacterium* of the present invention may effectively inhibit growth of the various pathogenic bacteria.

Example 6**Inhibition assay for salmonella**

[0103] *Salmonella* are bacteria that invade epithelial cells and multiply therein. For determining the inhibitory activity of the *Bifidobacteria* of the present invention towards *Salmonella typhimurium* the strain SL1344 and following procedure was used.

[0104] The pathogenic cells were cultivated in LB-medium. After the second passage to new medium the bacterial strains were marked with radioisotopes using C¹⁴-acetate at 10 µCi/ml in LB-medium. Incubation of the strains in this medium was performed for 18 hours at 37°C.

[0105] The bacterial suspension was subsequently subjected to centrifugation (1041 rpm, 15 min) so as to eliminate the remaining C¹⁴-acetate from the supernatant. The pellet was suspended and washed in PBS and the cells were suspended at a concentration of about 10⁸ cells / ml in 1% sterile mannose. Mannose is known to inhibit non-specific adhesion. The bacterial solution was then adjusted to 2 x 10⁸ cells/ml.

[0106] The pathogen (1 ml; 2 x 10⁸ cells) and an aliquot of a supernatant (1 ml) of a *Bifidobacterium* culture are pre-incubated for 2 hours at 37°C. The suspension is subsequently centrifuged, the resulting supernatant is removed and the pellet is again suspended in 0.5 ml PBS. This pathogen solution (0.5 ml) is then brought in contact with human intestinal cells in culture. The culture was washed with sterile PBS twice and 0.5 ml adhesion medium (DMEM) was added. The cells are then incubated for 1 hour at 37°C under 10% CO₂.

[0107] After incubation the number of bacteria in the incubation medium and on/in the intestinal cells are counted. In order to determine the amount of cells adhering on or having invaded into the intestinal cells the following approaches have been chosen.

[0108] For determining the number of adhering bacteria the medium was decanted and the cells were washed once with culture medium and once with sterile PBS. Subsequently, 1 ml of sterile H₂O was added per compartment, to lyse the cells and to form a cell solution which was incubated for 1-2 hours at 37°C, after which successive dilutions were carried out. In order to count the number of adhering and invasive bacteria, the cell solution was centrifuged to remove cell debris and the radioactivity was measured.

[0109] According to another protocol 10 aliquots were each put on TSA medium. The media were then incubated for 18-24 hours at 37°C.

[0110] For determining the amount of invaded bacteria the Caco-2 cells were washed with PBS so as to eliminate all non-adhering cells. Subsequently, a medium containing gentamycin (20 µg/ml) was added and incubation was continued for 1 hour at 37°C. Gentamycin is an antibiotic not penetrating intestinal cells so that all extracellular microorganisms were killed, while bacteria having already invaded intestinal cells will survive. The cells were then incubated for another hour at 37°C and were then washed twice with PBS. The cells were lysed by addition of and incubation in sterile distilled water for 1-2 hours at 37°C. After removing the cell debris radioactivity was determined. According to another protocol successive dilutions were carried out, which were put on TSA medium. Incubation: 18-24 hours at 37°C.

[0111] It may be seen that cultured cells and the culture supernatant were extremely effective in preventing adhesion of and invasion into intestinal cells by *Salmonella*.

Example 7**Infection of mice by the strain *S. typhimurium* C5**

[0112] Adult, 7-8 weeks old, axenic, female mice (C3H/He/oujco conventional, Iffa Credo, France), raised under sterile conditions, were orally infected with a fixed concentration of *S. typhimurium* (0,2 ml, 10^8 cfu/mouse). Some mice were rendered monoxenic by the implantation of a range of Bifidobacteria strains. With some mice, the Bifidobacteria in segments of the intestine were counted after its removal and mincing of the organs in PBS. With other mice, the protection against infection was assessed in such a way that they were continuously kept in a sterile environment and the days of survival were compared to the control group.

[0113] The results are shown in Fig. 4. As may be derived therefrom in the control group nearly all mice died after a time period of about 10 days. In contrast thereto, all mice treated with NCC2705 were alive after 10 days with only 20 % dying from the detrimental effect exerted by Salmonella after a period of 30 days.

Example 81st protocol:

[0114] 30 µl of the respective bacterial suspension (containing on average 3×10^6 bacteria) were mixed with 70 µl M199 medium supplemented with 10% tryptose phosphate broth (Flow) and 5% trypsin-EDTA solution (Seromed) to which were added 100 µl of virus in supplemented M199 medium. The virus-bacteria mixture thus obtained was incubated for 1 hour at 4°C and for 1 hour at 37°C. Separately, cells of the human undifferentiated colon adenoma cells HT-29 growing as a confluent monolayer in 96-well microtiter plates (in M199 medium supplemented with 10% tryptose phosphate broth (Flow) and 5% trypsin-EDTA solution (Seromed) 1 : 4 diluted with PBS) were washed three times with phosphate-buffered saline (PBS ; pH 7.2). The virus-bacteria mixture processed as indicated above was transferred to the cells and the microtiter plates were incubated for 18 h in a CO₂ incubator (Heraeus). Virus replication was assayed as described below.

2nd protocol:

[0115] 30 µl of the bacterial suspension (supra) were mixed with 70 µl M199 medium supplemented with 10% tryptose phosphate broth (Flow) and 5% trypsin-EDTA solution (Seromed) and applied directly on HT-29 cells grown and pre-treated as described in the 1st protocol in the microtiter plates. After one hour incubation at 37°C 100 µl of virus in supplemented M199 medium were added to the cells in the microtiter plates. The incubation was continued for 18 h in a CO₂ incubator (Heraeus). Virus replication was assayed as described below.

[0116] The rotavirus replication was assessed by histo-immunological staining of rotavirus proteins in infected cells as described hereafter.

[0117] One day after infection, the cell culture medium was removed from the microtiter plates and the cells were fixed with absolute ethanol for 10 min. Ethanol was discarded, and the plates were washed three times in PBS buffer. Then 50 µl of an anti-rotavirus serum (mainly directed against VP6 protein), produced in rabbits (obtained from the ISREC University of Lausanne) and diluted 1 : 2000 in PBS was added to each well and incubated for 1 h at 37°C with a cover slip to prevent desiccation of the wells. The anti-serum was discarded afterwards and the plates were washed three times with PBS. Then 50 µl of anti-rabbit immunoglobulin G (IgG) antiserum produced in goats and coupled to peroxidase (GAR-IgG-PO; Nordic) were added at a dilution of 1 : 500 in PBS to each well and the plates were incubated for 1 hour at 37°C. The serum was discarded and the plates were again washed three times with PBS. Then 100 µl of the following substrate mixture was added to each well: 10 ml of 0.05 M Tris-hydrochloride (pH 7.8), 1 ml of H₂O₂ (30% suprapur, diluted 1 : 600 in H₂O ; Merck) and 200 µl of 3-amino-9-ethylcarbazole (0.1 g/10 ml of ethanol stored in 200 µl aliquots at -80 °C ; A-5754 ; Sigma). The plates were incubated for at least 30 min at room temperature. The substrate was discarded and the wells were filled with 200 µl of H₂O to stop the reaction. Infected cell foci were counted with an inverted microscope (Diavert; Leitz).

[0118] Only very few bacterial strains interacted with rotaviruses. Merely 4 out of the 260 bacterial cells primarily selected inhibited rotavirus replication in at least one protocol. Bifidobacterium adolescentis CNCM I-2618 (NCC2705) showed an extremely high activity against Serotype 1 Rotavirus, Serotype 3 rotavirus SA-11 and Serotype 4 rotavirus Hachi.

[0119] NCC2705 is gram positive and catalase negative, it does not produce CO₂ during fermentation and produces just L (+) lactic acid according to methods disclosed in the "Genera of lactic acid bacteria", Ed. B.J.B. Wood and W.H. Holzappel, Blackie A&P.

[0120] These results show the extreme superior properties of the Bifidobacterium of the present invention.

Claims

1. A polynucleotide having a nucleotide sequence of the Bifidobacterium genome, comprising
 - (a) the nucleotide sequence of SEQ. ID. No. 1;
 - (b) a nucleotide sequence exhibiting at least 90% identity with the sequence of SEQ. ID. No. 1; or
 - (c) a nucleotide sequence that hybridizes to SEQ. ID. No. 1 under stringent conditions.
2. A polynucleotide having a nucleotide sequence selected from the group:
 - (a) a nucleotide sequence as identified by SEQ. ID. NO. 1099; or
 - (b) a nucleotide sequence exhibiting at least 95 % identity with SEQ. ID. NO. 1099; or
 - (c) a polynucleotide which hybridizes to SEQ. ID. NO. 1099 under conditions of high stringency.
3. A polynucleotide having a nucleotide sequence of an open reading frame (ORF) of a Bifidobacterium longum genome, comprising:
 - (a) a nucleotide sequence chosen from any one of Seq ID. No. 2 to SEQ. ID. NO. 1098; or
 - (b) a nucleotide sequence exhibiting at least 95 % identity with any one of SEQ. ID. NO. 2 to SEQ. ID. NO. 1098; or
 - (c) a polynucleotide which hybridizes to any one of SEQ. ID. NO. 2 to SEQ. ID. NO. 1098 under conditions of high stringency.
4. The polynucleotide of any of the claims 1 or 2, which encodes the following polypeptides or fragments thereof:

(a) SEQ. ID. No.5 (ORF13)

MPTGRVRWFDAAKGYGFITSEEGKDVFLPAQALPTGVTTTLRKGAKVEYSV
 VDGRRGPPQAMDVRLIASAPSLVKATRPKADDMAAICEDLIKMLDAAGNTL
 RRHRYPSAADSKKLATLLRAVADQFDVQD

(b) SEQ. ID. No.525 (ORF1827)

5 MTTAAQAPAPGKLEFKDDYTPDEAERVIRNSKGLPVGVRPKMVWTWKA
 LLWAAIAIVCACGWAILAVSRGEQISAIWFLVVALSSYAIAVRFYAYYIQ
 10 IKIMRTDDANATPAERVHDGANFERTDRRVLFQGHFAGISGAGPLVGPIL
 AAQMGYLPSTLWIIILGVIFAGAVQDMLVLWISAKRRGRSLGQMATDEMKG
 FGGMILSIFLVVMTAIAMAFLALVAIKAMAASPWAVFSIGMTIPIALIMG
 15 CYQRFLRPGRVIETTLGFEVLLVLDIVAGGWIASIPAVAAVFTLDAKQLV
 IALVIYSFAAAALPHWLLVTPRDYLTLMKIGTLVLLVIGIIIANPSVKV
 PGLTELASTSTGPTFSGNLFPLFITIACGALSGFHGAVSSGLTPKAVEK
 20 ENQIRMIGYGSMVESFTAVIALIAAITISQGVYFSTNMSAAQITAASGV
 SISATSTPGEQADA AVKAVESMKVSDIEGNQMQVTWDSVDENGAAKTYEG
 AAALQAAADIGETSIVSRTGGATTfamGMANFLKSYLGGHDSMAFWYHF
 25 AIMFEALFILTTVDNGTRVARYQIGEMLGNVRKLKKFADPTWKPGNIITT
 LIATALWGGLLWMGVSDANGGINAMVPIFGISNQLLAAACFVLITVCVAK
 MGYWKHLWIPVVPLVWDIAVTFTADFQKIFGPLSYFTTASKYQAQIDSGE
 30 LTGEALTNAAALSNAAYLDGVLVSVFFLVMMGVFVVVGIVVVARTFAAGKY
 GAETTSEEPFVESQWFAPSSLVATALEKKVQREYSAKLHELVRNGQVAA

c) SEQ. ID. No.424 (ORF1473)

35 MTQSRRLVLRVVEDYIRSQEPVGSTSLTRDHD LGVSSATIRNDMAALE
 40 DEGYLIQPHTSAGRVPTTEKGYRYFVDRLATVVPLSEAQR RGINSFLSGSV
 SLKDALQRSARLLSEITGQVAVVASPSLAKATLRHVEMVPVAMTTLLAVV
 ITDTGRVAQHGLTIASMPAVDEINRLSNTVNEQCDGLSLSKSAETVRSIA
 45 ASAGYESVRGVADTLADAFESMALDERANELYMSGTSHLAHSRSLADLAP
 LFDAL EEQVVLMLKMSNLSEETNASGVGVAIGSEMHTPGLLHASVVSSGY
 50 GRSGAAGEPAGNDPVGEPETESETESQTNDEPIAFVGSIGPTHMDYAAT
 MAAVRVARYLTAFLSEGRTQD

d) SEQ. ID. No.548 (ORF1905)

55 MYFKDGNDNAQRGGSTVRRSRQRRIMGRVVSYNEDVPRCTFCGKTEHQVR

EP 1 227 152 A1

KL VAGPNASICDECIALCVDII SEERVKDAEVNSLSLPKPAQIFDYLNRY
VIGQENAKRALSVAVYNHYKRVNMELQESAEQLDGNNGHSGQTSKQAKQS
5 VPTQTRATRRSNDPLADVEVAKSNILLGPTGVGKTYLAQALARVMNVPP
VITDATTLTEAGYVGDDVETVLQRLLQAADGDVSRAQHGI IYIDEIDKIA
RKSGENTSITRDVSGEGVQQALLKILEGTIASVPLEGTRKHKEQDVAQMD
10 TRGILFICGGAFFVGLTDIVRKRLGRRETGFGANWHDADMKDEELLEQVNA
DDLAEFGLLPEFIGRLPVTSVLKELTVDDLTAILTQPANALIKQYRKLFA
VDGVDLQFTEQAIRAIADIAIKQGTGARGLSIIERTLQDTMFQLPSLDD
15 VRQVIVDKASVEGSSTPKLLREAVDVPQGRLLKVAQSVLLDRVRTHEA

e) SEQ. ID. No.74 (ORF219)

MSEQLMEQYRLRGQRKCRNACIAAIVTVVLVLAVAGGVWWTAGDGSALVR
25 NMFKPKATPATQPVVNSTATFAYRTAPEFLAMEAGDRGTGNVNYSPASMW
MALAIAAQGANGTTRSQNLNELLGSGSLTDSQYQSLSSINGQYSGAKSEM
SAANSLWIDDDYSLASDYQSTVKMFEEAEVTTLPFDDQAAAKMSDWIAKH
30 TNGSLKPKITLRDREVL SIINTVYADGRWKDPFEEQSTGNGTFHGEAGDA
QVPMMHQTFSQMAYGHDEYNTWQORVEI PFDNGGNLAI VLPAGHFDELAG
DAEKLSWAFGTCSTASLGEGAMGCAADSM PGWGVSVNSVMNVNVTLPRTI
35 DSMFDSEATIKAFEKLGVTDAFSAGDADF TKMIDTGSHGENLYIGSILQG
TRIEVNEAGAKAMSFTKVGADSVSAPVDNVEFTVDRPFLYSYVTPDGIPL
FIGAVRN LGGVGGEN
40

f) SEQ. ID. No.576 (ORF1972)

5 MQIRPGSMYPLGASYDGAGVNFALYSQVAQKVELCLFDEHDVETRIEMTE
RNSYVWHNYI PGLHPGQRYGYRVYGPYDPVHGLRCNPNKLLLDPYAKAIE
10 GNIDGDESLFSYWFKSPDDNSAMNDLDSAAHTMKSAVINPYFDWGNDQHP
YISYHDSVIYEAHVRGMTNLNMDVPPDIRGTYAGLAYPSVIEYLLKLGIT
AIELMPIHQFVNDSFLQEKGLSNYWGYNITIGFFAPHNAYSSSGERGEQVN
15 EFKSMVKAYHRAGMEVILDVVYNHTAEGNHMGPTLSFKGIDNASYYRLVE
GDQQHYFDTTGTGNSLLMRSPHALQLITDSLRYWVTEMHVDGFRFDLAAT
LARQFQEVDKLSAFFDIVEQDPIISRVKLIAEPWDLGSGGYQVGGFPSSW

20 SEWNGRYRDTVRDFWRSQPSTLPEFASRLMGSSDLYQVNGRRPVASVNFI
TAHDGFTMNDLVSYNEKHNEANGEGNRDGESNNRSWNCGVEGPTNIPDVN
25 DLQRQMRNMFATLLFSQGI PMICGGDEVARTQQGNNNAYCQDNEISWTN
WHLDKGRKELLAFVSKLIHLRLDHPVLHRRRFFTGREP GDDSNTIPQVEW
FDHTGSIMDMDDWQNTAFSMMIYLNGSDIPEVDWYGNRMVDNDFILIFN
30 AHYEPIMFTLPDERYGRKWQLVVDTHNPNEPALSYEAGFMITAQSR SFLM
LMSAKKPKKPMGL

g) SEQ. ID. No.403 (ORF1403)

35 MEIRARPHMASGSYRELF SARM MYGMQYIQQTIVGIDGSEARFFGYVADN
40 SEEMEPDRIRPAILILPGGGYAMTSDREAEPVALQFLAKGFVAVFLRYSV
QPSRYPVALLEAAEAMRLIRANVDQWHVNPAQVAVLGFSAGGH LANLAT
45 SVGDEDIREQGGMDPDAVRPNALMLSYPVITAGKYAHRGSFQCLLGDAQH
NQALLDKFSIEKHIDAKTPPVFVWHTMTDDAVPVENTLMMLIQACRAAGVS
IEAHLFPEGSHGLSLANAETAGNGFYAHIVECVQCWPD LAEAWLRRLF
50

(h) SEQ. ID. No.804 (ORF2676)

5 MFLKPEQQLERCRRIVRQRVDPHIHPSIAQLTVESYDIPGEPMPSPDEFFA
KLDRGDIDFKPFMLGSEWGTTWGTWVFRLTGTVPAGYPKGKPLELILDG
WYPHSCGGHIEGLVYRADGTAIKAVHPLNYWVPFMDAEGNAQVPVAEDGS
10 FTLYLEAASNPLLLGVPPFIETELGDHATGKPDEPYVFKSADLAEFDERY
ENYSVDLDVVSSLMEFADKQSPRYWQLAKALQRLNAYDERNPESVEAAR
AVLAGVLAKPANASAMNVSAGHAHIDSAWLWPVRETRRKVARTVSNALA
15 LMDADPDFKYAMSSAQQYAWLEEDHPDIFKRMKRRIEGRFIPVGGMWVE
ADGMLPAGESLIRQIAYGRKYFKEHLGVEPKGVWLPDSFGYTGAWPQIAR
RAGYEWFLTQKISWNDTTKFPHHSFMWEGIDGSRIPTHFPPADTYAAWCK
20 VQELDYAEKNFQDKDLSDRSLLLFGFGDGGGGPTRNMMEHLHRYENLEGV
SKVSIEEPNDFFDKAHQQLAENAGPEMPVWKGELYLELHRGTLTSQQDMK
RGCRRQEESSLRTVEYLGAAAVLSDPEYVYPREELDRIWKTLLLNQFHDIL
25 PGSAIAWVHREAREDYRRDLKRLAEIAQDMCAVLRKANPQADLLAEARIS
QFRNDGASWHANRINEPTDALSVLTQTLDNQGRVLLANGVLSVTIEADGTI
30
SSLLDEEHGRELVPACTRLGQYELLRDEPAVWDAWEIERESLLMANAVTG
SIESVNTENGAAQVHVHTADGDTVITTTITLRPGSHTLDFHADIDWHERE
35 RFLKVDLPLGIVADQATYDCQYGLIRRPVKN TASDEAKYESSTNRFAI I
GDAGYAAAVINGSVYGS DASPIAGNAEGRDSGTMFRLSLLSAPTFPDPR
TDIGSHEFDWSV VADATVDRALDAAGVLNAPVLHDVPDITPLASIESVNG
40 TVVLDWMKLADDGSGDLIVRAYEAAGGQADAMLHVCPALAGASVHETNVL
EGDDLAADLPVALQDGRQNAEGATLHFGPFQLATLRITR
45
50
55

(i) SEQ. ID. No.313 (ORF1077)

MISRDGWAVIDDSAANII IETDTVNGKANPFGTWVSPRATAETDLYFFGY
 GHRYIEAVRDFYRLTGPTLLPRFAMGNWWSRYRYTQDGYLALMDRFKR
 EGIPFTTSVIDMDWHRVDDVDPKYGSGWTGYSWNRELPDPPAFLADLHR
 RGLRTTLNVHPRDGVRAFEDAYPEVAKRVGIDPATEENVEFDLTNPDFVD
 AYFDMHHRMEAEGVDFWWLDWQQGGVTRQKGLDPLWMLNHMHYLDSGRGG
 NWPLTFSRYAGPGSHRYPVGFSGDTIVTWESLAFQPQFTATASNIGYGW
 SHDIGGHMFGYRNEELEARWYQLGAFSPINRLHSSNSPFSGKEPWNFNRD
 VSAAMVDALRLRHAMMPYLYTMNYRAAEAGRPLVEPMYWQNPDPDAYEV
 PDEFRFGTELVVAFIVSPDDAAACRGRADAWLPQGEWFDFFDGRRYVSSD
 AAGRRLEVWRS�DRTPVFAKAGAIVPLQDVAESGEAINSIANPQALRVLV
 FPGADGSFVMREDRGTWGA PSADTAIAFTWGGADASPSAFTVAPVTGDT
 AVPELRDWTVVFRGVAPVDAASGVRAWSGEAPVEATVAYDEATMSLTVSV
 TGISSAASLRIEIPGGLRIADNPVESDAMDLLLHAQMLYRTKELALQAVH
 KLGIGAIGALRTMNRGPYANDFWITDMPDAVAGALEEILLRS

5. A polynucleotide encoding a fusion protein, comprising any one of SEQ. ID. NO. 2 to SEQ. ID. NO. 1098 ligated in frame to a polynucleotide encoding a heterologous polypeptide.
6. A recombinant vector that contains the polynucleotide of any of the preceding claims.
7. A recombinant vector according to claim 6, that contains a polynucleotide of Claim 4.
8. A recombinant vector according to any of the claims 6 or 7, wherein the polynucleotide is operatively associated with a regulatory sequence that controls gene expression.
9. A host that contains a polynucleotide according to any of the Claim 1 to 5 or a recombinant vector according to any of the claims 6 to 8.
10. A host according to claim 9, that contains a polynucleotide of Claim 4 or the vector according to claim 7.
11. A host according to any of the claims 9 or 10, which is a procaryotic cell, an eucaryotic or a plant or a non-human animal.
12. A method for producing a polypeptide of *Bifidobacterium longum*, comprising:
 - (a) culturing a host cell according to claim 9 or claim 10 under conditions suitable to produce the polypeptide encoded by the polynucleotide; and
 - (b) recovering the polypeptide from the culture.
13. A method for producing a fusion protein, comprising:
 - (a) culturing a host cell according to Claim 9 or claim 10 under conditions suitable to produce the fusion protein encoded by the polynucleotide; and

(b) recovering the fusion protein from the culture.

14. A polypeptide encoded by a polynucleotide according to any of the claims 3 to 5.

15. A fusion protein encoded by a polynucleotide of Claim 5.

16. An antibody that immunospecifically binds to a polypeptide of any of the claims 14 or 15.

17. An antibody that immunospecifically binds to the fusion protein of claim 5.

18. A method for the detection and/or identification of *Bifidobacterium longum* in a biological sample, comprising:

- (a) contacting the sample with a polynucleotide primer derived from a sequence according to any of the claims 1 to 4 in the presence of a polymerase enzyme and nucleotides under conditions which permit primer extension; and
- (b) detecting the presence of primer extension products in the sample in which the detection of primer extension products indicates the presence of *Bifidobacterium longum* in the sample.

19. A method for the detection and/or identification of *Bifidobacterium* in a biological sample, comprising:

- (a) contacting the sample with a probe derived from a polynucleotide according to any of the claims 1 to 8 under conditions which permit hybridization of complementary base pairs; and
- (b) detecting the presence of hybridization complexes in the sample in which the detection of hybridization complexes indicates the presence of *Bifidobacterium longum* in the sample.

20. A method for the detection and/or identification of *Bifidobacterium* in a biological sample, comprising:

- (a) contacting the sample with an antibody according to Claim 16 or 17 under conditions suitable for the formation of immune complexes; and
- (b) detecting the presence of immune complexes in the sample, in which the detection of immune complexes indicates the presence of *Bifidobacterium longum* in the sample.

21. A method for the detection and/or identification of antibodies to *Bifidobacterium longum* in a biological sample, comprising:

- (a) contacting the sample with a polypeptide according to any of the claims 14 or 15 under conditions suitable for the formation of immune complexes; and
- (b) detecting the presence of immune complexes in the sample, in which the detection of immune complexes indicates the presence of *Bifidobacterium longum* in the sample.

22. A DNA array/chip containing an array of polynucleotides comprising at least a polynucleotide according to any of the claims 1 to 4 or a vector according to any of the claims 6 to 8.

23. A protein array/chip containing an array of polypeptides comprising at least one of the polypeptides according to any of the claims 14 or 15.

24. An immunogenic composition comprising a polypeptide according to any of the claims 14 or 15 and a pharmaceutically acceptable carrier.

25. An immunogenic composition comprising a polypeptide according to any of the claims 14 or 15 and a pharmaceutically acceptable carrier.

26. A screening assay, comprising:

- (a) contacting a test compound with a polynucleotide according to any of the claims 1 to 4 or a vector according to any of the claims 6 to 8; and
- (b) detecting whether binding occurs.

27. A screening assay, comprising:

- (a) contacting a test compound with a polypeptide according to any of the claims 14 or 15; and
- (b) detecting whether binding occurs.

28. A kit comprising a container containing a polynucleotide according to any of the claims 1 to 4.

29. The kit according to claim 28, wherein the polynucleotide is a primer or a probe and wherein the kit optionally contains a polymerase and deoxynucleotide triphosphates.

30. A kit comprising a container containing an antibody that immunospecifically binds to a polypeptide according to any of the claims 14 and 15.

31. A computer readable medium having recorded thereon a nucleic acid sequence according to any of the claims 1 to 8.

32. A computer readable medium having recorded thereon a polypeptide sequence according to any of the claims 14 or 15.

33. The computer readable medium according to any of the claims 31 or 32, wherein said medium is selected from the group consisting of:

- (a) a floppy disc;
- (b) a hard disc;
- (c) random access memory (RAM);
- (d) read only memory (ROM); and
- (e) CD-ROM.

34. A computer-based system for identifying fragments of the *Bifidobacterium longum* genome comprising the following elements:

- (a) a data storage means comprising a nucleic acid sequence according to any of the claims 1 to 4;
- (b) search means for comparing a target sequence to the nucleotide sequence of the data storage means of step (a) to identify homologous sequence (s); and
- (c) retrieval means for obtaining said homologous sequence (s) of step (b).

35. Lactic acid bacterium, which is *Bifidobacterium* NCC2705 (CNCM I-2618).

36. Use of the *Bifidobacterium* according to claim 35, or a culture supernatant thereof, or a metabolite thereof for the preparation of a carrier.

37. The use according to claim 36, wherein the *Bifidobacterium* is contained in the carrier in an amount of from about 10^5 cfu / g to about 10^{12} cfu / g carrier material.

38. The use according to any of the claims 36 and 37, wherein the carrier is for the prevention and/or treatment of diarrhea brought about by pathogenic bacteria and/or rotaviruses.

39. The use according to any of the claims 36 to 38, wherein the carrier is a food composition selected from milk, yogurt, curd, cheese, fermented milks, milk based fermented products, ice-creams, fermented cereal based products, milk based powders, infant formulae, pet food or a pharmaceutical composition selected from tablets, liquid bacterial suspensions, dried oral supplement, wet oral supplement, dry tube feeding or wet tube feeding.

ADHESION OF HUMAN BIFIDOBACTERIA ONTO CULTURED HUMAN COLONIC CRYPT T84 CELLS

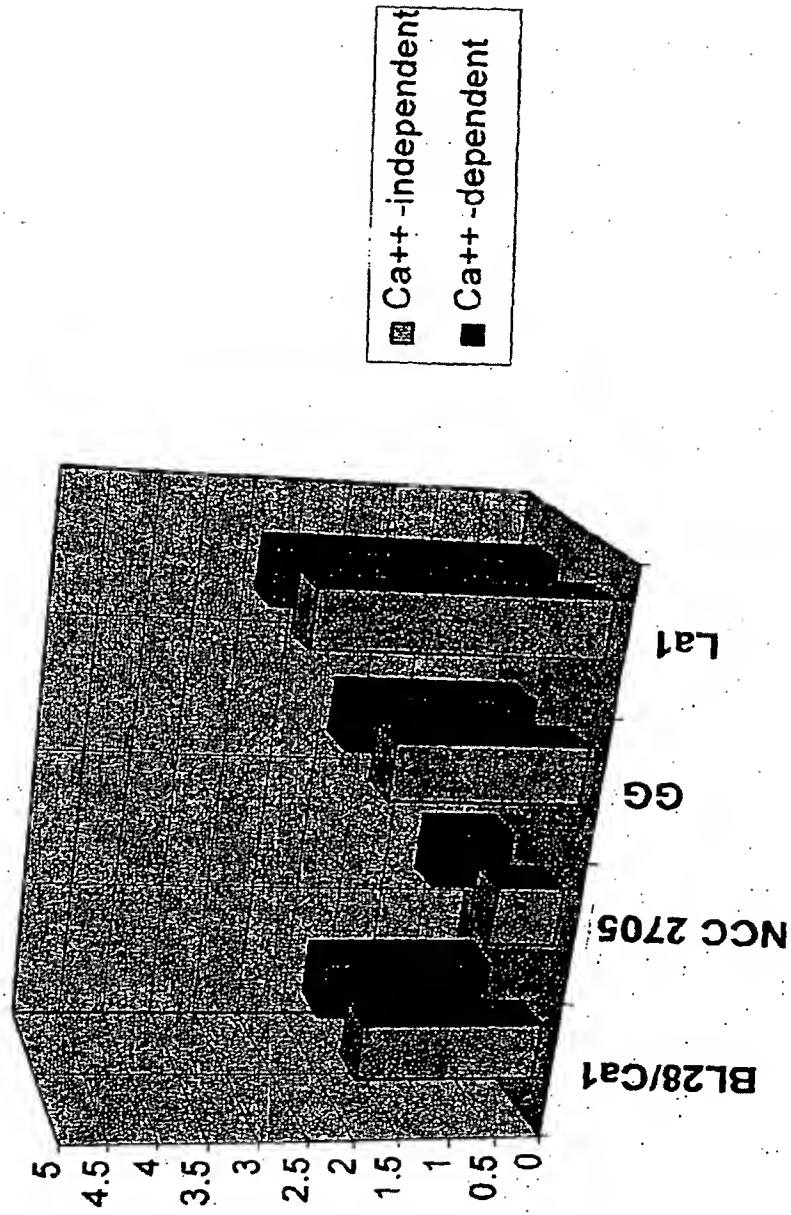


FIG. 1

PATHOGENS SENSITIVITY TO HUMAN BIFIDOBACTERIA NCC 2705

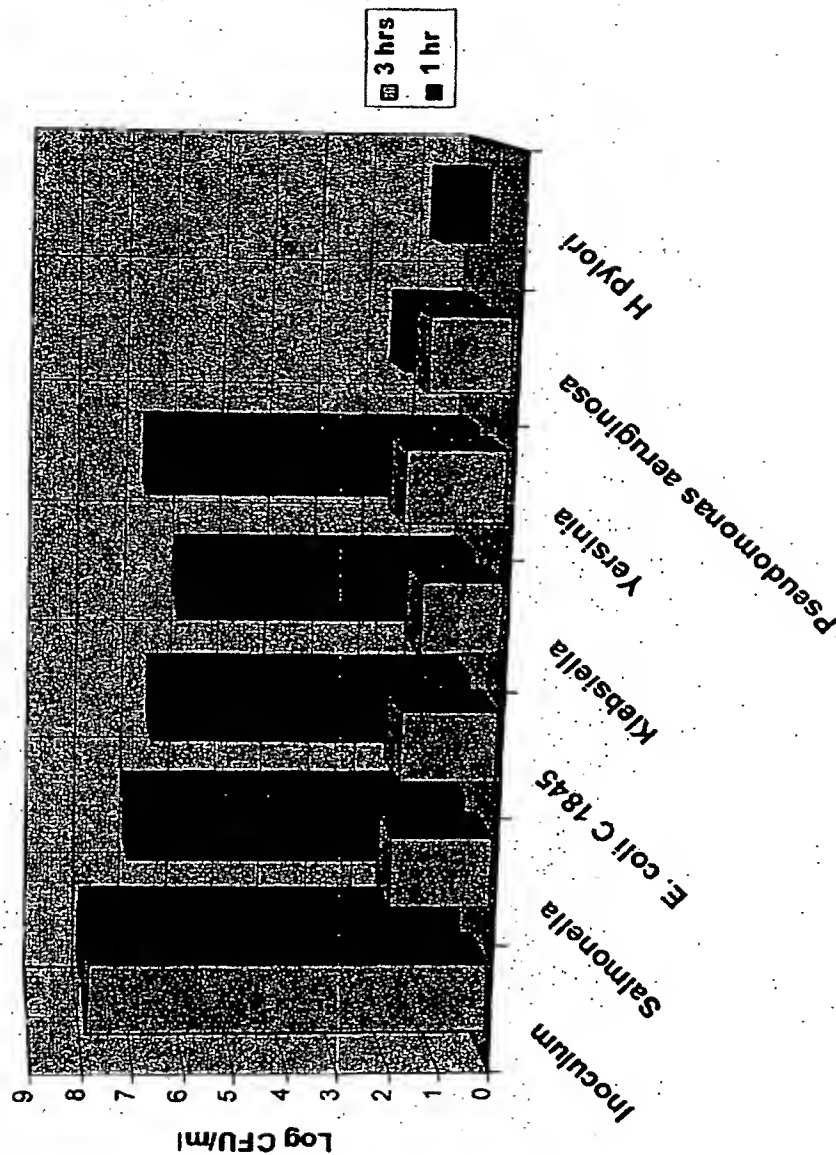


FIG. 2

**ACTIVITY OF HUMAN BIFIDOBACTERIA BL28/CA1 AND NCC 2705
AGAINST *S. TYPHIMURIUM* SL 1344
INFECTING ENTEROCYTE-LIKE Caco-2 CELLS**

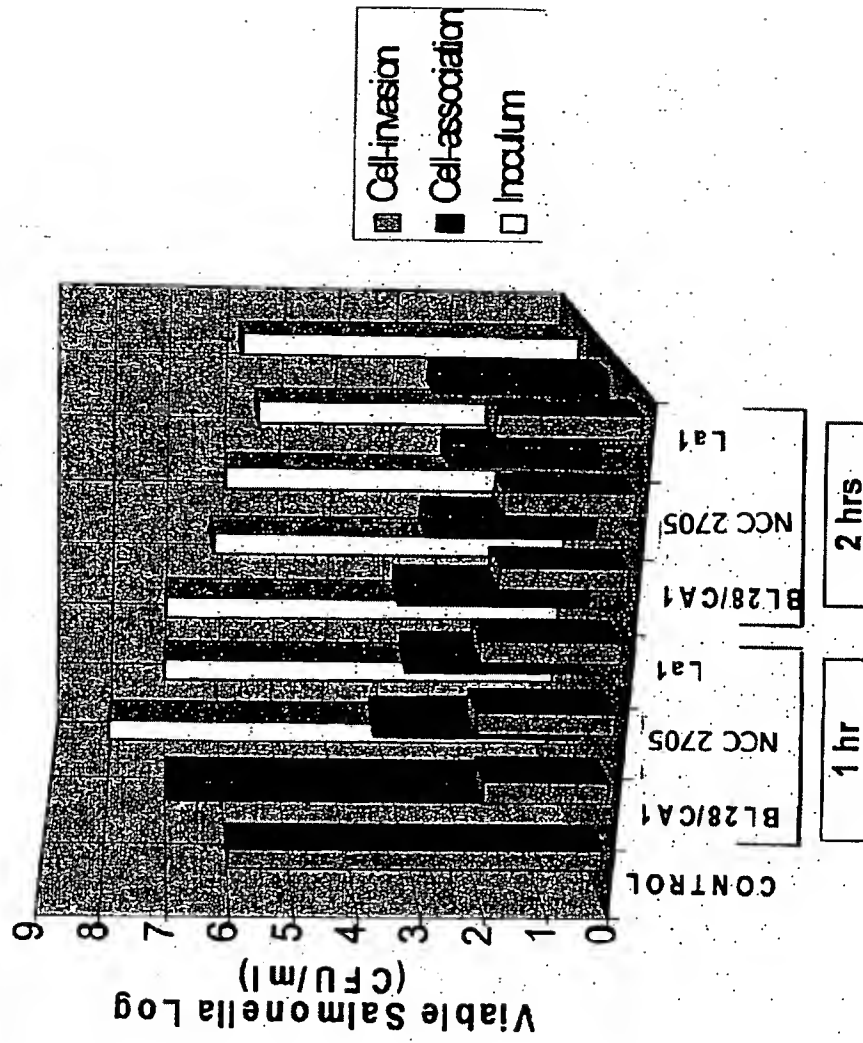


FIG. 3

ACTIVITY OF INFANT BIFIDOBACTERIA AGAINST S. TYPHIMURIUM IN VIVO

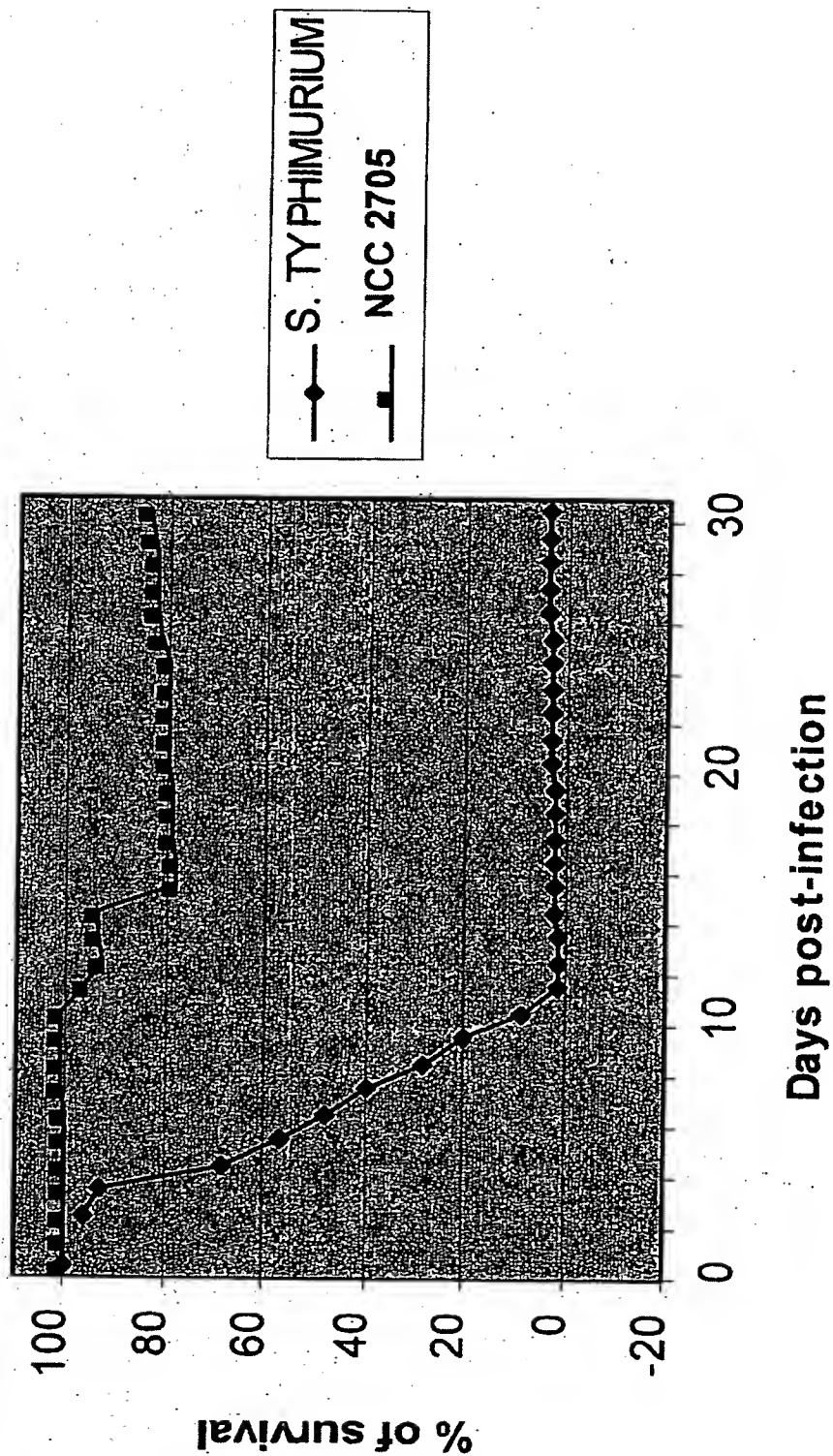


FIG. 4

Cell Culture Screening

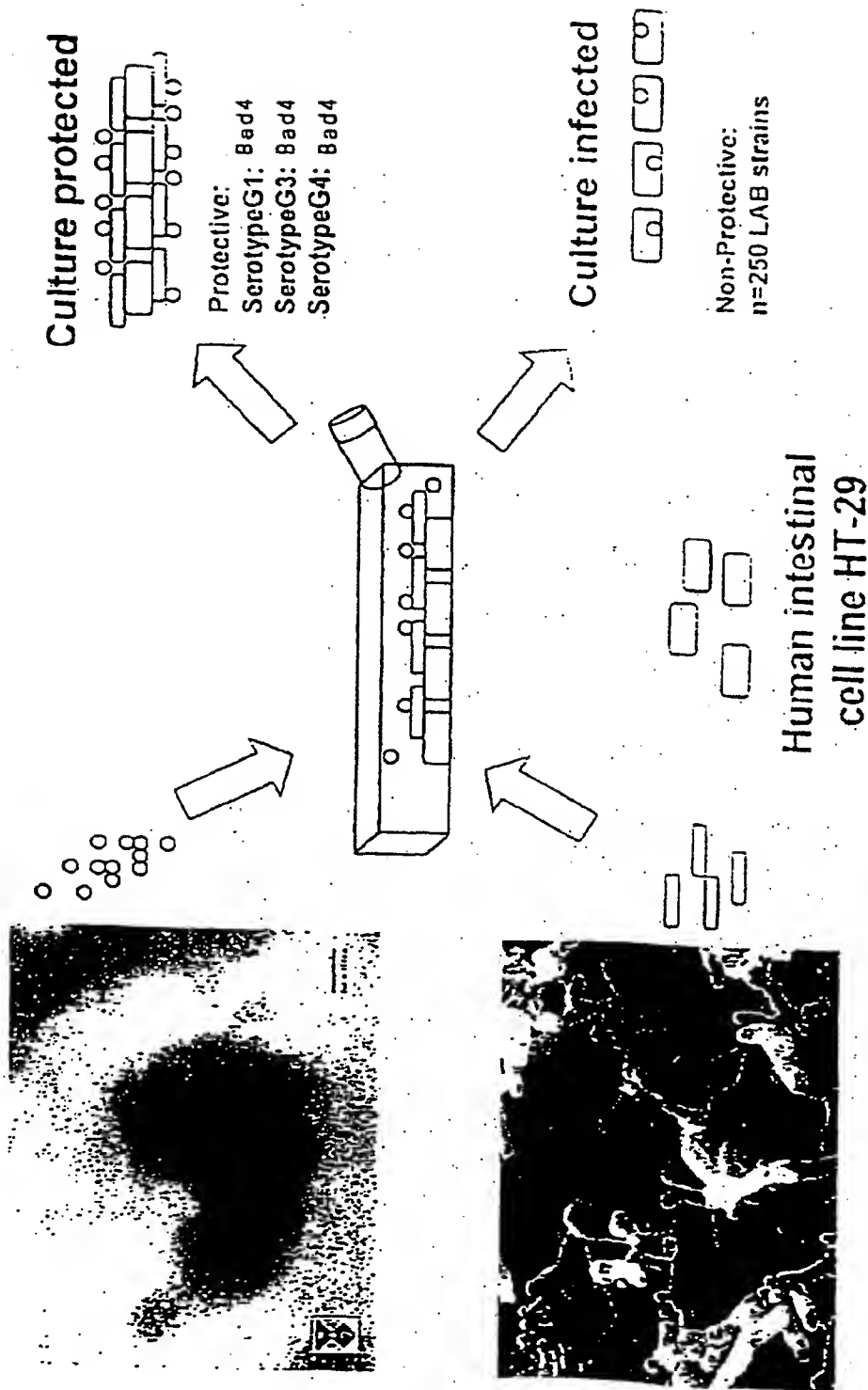


FIG. 5

European Patent
Office

EUROPEAN SEARCH REPORT

Application Number
EP 01 10 2050

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
1 X	DATABASE EMBL [Online] EBI AY004282, 2 January 2001 (2001-01-02) JIAN W. ET AL: "Bifidobacterium animalis strain DSM10140 heat shock protein 60 gene" XP002177946 * the whole document *	1,6,8,9, 11-13, 18,19, 22,26, 28,29	C12N15/31 C12N1/20 C07K14/195 C07K16/12 C12Q1/68 A61K39/02 G01N33/53 G06F19/00 C12R1/01
X	-& DATABASE EMBL [Online] EBI SEQ. ID. NO.: 1/AY004282 ALIGNMENT, XP002177947 * the whole document *	1,6,8,9, 11-13, 18,19, 22,26, 28,29	//(C12N1/20, C12R1:01)
1 X	DATABASE EMBL [Online] EBI AF210319, 21 December 1999 (1999-12-21) JAN W. ET AL: "Bifidobacterium adolescentis heat shock protein 60 gene" XP002177948 * the whole document *	1,6,8,9, 11-13, 18,19, 22,26, 28,29	
X	-& DATABASE EMBL [Online] EBI SEQ. ID. NO.: 1/AF210319 ALIGNMENT, XP002177949 * the whole document *	1,6,8,9, 11-13, 18,19, 22,26, 28,29	TECHNICAL FIELDS SEARCHED (Int.Cl.7) C07K C12N G06F A61K G01N
-/--			
The present search report has been drawn up for all claims			
Place of search MUNICH		Date of completion of the search 2 October 2001	Examiner Celler, J
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document	

EPO FORM 1503 03.82 (P04C01)



European Patent
Office

EUROPEAN SEARCH REPORT

Application Number

EP 01 10 2050

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
1 X	DATABASE EMBL [Online] EBI AF210319, 21 December 1999 (1999-12-21) JAN W. ET AL: "Bifidobacterium adolescentis heat shock protein 60 gene" XP002177950 * the whole document *	1,6,8,9, 11-13, 18,19, 22,26, 28,29	
X	-& DATABASE EMBL [Online] EBI SEQ. ID. NO.: 1/AF210319 ALIGNMENT, XP002177951 * the whole document *	1,6,8,9, 11-13, 18,19, 22,26, 28,29	
1 X	DATABASE EMBL [Online] EBI AF240565, 16 March 2000 (2000-03-16) JIAN W. ET AL: "Bifidobacterium denticolens heat shock protein 60 gene" XP002177952 * the whole document *	1,6,8,9, 11-13, 18,19, 22,26, 28,29	
X	-& DATABASE EMBL [Online] ebi SEQ. ID. NO.: 1/AF240565, XP002177953 * the whole document *	1,6,8,9, 11-13, 18,19, 22,26, 28,29	
			TECHNICAL FIELDS SEARCHED (Int.Cl.7)
<p>--- -/--</p>			
The present search report has been drawn up for all claims			
Place of search MUNICH		Date of completion of the search 2 October 2001	Examiner Celler, J
CATEGORY OF CITED DOCUMENTS		<p>T: theory or principle underlying the invention E: earlier patent document, but published on, or after the filing date D: document cited in the application L: document cited for other reasons * & : member of the same patent family, corresponding document</p>	
<p>X: particularly relevant if taken alone Y: particularly relevant if combined with another document of the same category A: technological background O: non-written disclosure P: intermediate document</p>			

EPO FORM 1503 03.82 (P04C01)



European Patent
Office

EUROPEAN SEARCH REPORT

Application Number
EP 01 10 2050

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
1 Y	DATABASE EMBL [Online] EBI AF240579, 16 March 2000 (2000-03-16) JIAN W. ET AL: "Gardnerella vaginalis heat shock protein 60 gene" XP002177954 * the whole document *	1,6,8,9, 11-13, 18,19, 22,26, 28,29	
Y	-& DATABASE EMBL [Online] EBI SEQ. ID. NO.: 1/AF240579 ALIGNMENT, XP002177955 * the whole document *	1,6,8,9, 11-13, 18,19, 22,26, 28,29	
1 X	DATABASE EMBL [Online] EBI AY004281, 2 January 2001 (2001-01-02) JIAN W. ET AL: "Bifidobacterium inopinatum" XP002177956 * the whole document *	1,6,8,9, 11-13, 18,19, 22,26, 28,29	
X	-& DATABASE EMBL [Online] EBI SEQ. ID. NO.: 1/AY004281 ALIGNMENT, XP002177957 * the whole document *	1,6,8,9, 11-13, 18,19, 22,26, 28,29	
3 X	TOMB J-F ET AL: "THE COMPLETE GENOME SEQUENCE OF THE GASTRIC PATHOGEN HELICOBACTER PYLORI" NATURE, MACMILLAN JOURNALS LTD. LONDON, GB, vol. 388, no. 6642, 7 August 1997 (1997-08-07), pages 539-547, TABEL, XP002062106 ISSN: 0028-0836 * abstract *	1,6,8,9, 11-13, 18,19, 22,26, 28,29	TECHNICAL FIELDS SEARCHED (Int.Cl.7)
-The present search report has been drawn up for all claims			
Place of search MUNICH		Date of completion of the search 2 October 2001	Examiner Celler, J
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document			

EPO FORM 1503 (03.02) (P04C01)

European Patent
OfficeLACK OF UNITY OF INVENTION
SHEET B

Application Number

EP 01 10 2050

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

Invention 1 (Claims 1,6,8,9,11-13,18,19,22,26,28, 29 partly)

-A polynucleotide having a nucleotide sequence of the Bifidobacterium, comprising the nucleotide sequence of SEQ. ID. NO.: 1, a nucleotide sequence exhibiting at least 90% identity with the SEQ. ID. NO.: 1 or a nucleotide sequence that hybridises to SEQ. ID. NO.: 1 under stringent conditions, a recombinant vector that contains a polynucleotide as above, a host that contains polynucleotide as above or a vector as above, a method of producing a polypeptide of Bifidobacterium longum and a fusion polypeptide thereof, a method of detecting and/or identifying Bifidobacterium in biological sample with help of the polynucleotide as above, a DNA array/chip containing an array of polynucleotides comprising a polynucleotide as above, a screening assay for a compound binding to polynucleotide as above and a kit containing a nucleotide as above.

Invention 2 (Claims 2,6,8,9,11-13,18,19,22,26,28, 29 partly)

-A polynucleotide having a nucleotide sequence selected from the group: a nucleotide sequence as identified by SEQ. ID. NO. 1099 or a nucleotide sequence exhibiting at least 95% identity with SEQ. ID. NO.: 1099 or polynucleotide which hybridises to SEQ. ID. NO.: 1099 under conditions of high stringency, a recombinant vector that contains a polynucleotide as above, a host that contains a polynucleotide as above or a vector as above, a method of producing a polypeptide of Bifidobacterium longum and a fusion protein thereof, a method of detecting or identifying Bifidobacterium in biological samples with help of polynucleotides as above, a DNA array/chip containing an array of polynucleotides as above and a kit containing a nucleotide as above.

Invention 3 (Claims 3-6,8,9,11-30 partly)

-A polynucleotide having a nucleotide sequence of an open reading frame of Bifidobacterium longum genom comprising the nucleotide sequence SEQ. ID. NO.: 2, a nucleotide sequence exhibiting at least 95% identity with that encoding SEQ. ID. NO.: 2, a nucleotide sequence that hybridises to that encoding SEQ. ID. NO.: 2 under stringent conditions, a polynucleotide encoding a fusion protein of that of SEQ. ID.



The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

NO.: 2 and a heterologous polypeptide; a corresponding recombinant vectors and hosts, a method of producing a polypeptide of SEQ ID NO.: 2 and said fusion polypeptide, polypeptides and fusion polypeptides characterised by SEQ. ID. NO.:2, corresponding immunospecific antibodies, a method of detection and/or identification of Bifidobacterium in biological samples based on said nucleic acids, polypeptides and/or antibodies, a DNA array/chip containing an array of polynucleotides comprising a polynucleotide encoding the SEQ. ID. NO.:2, having at least 90% identity to that encoding SEQ. ID. NO.: 2 or hybridising under high stringency with such a sequence or comprising corresponding vector, a protein chip/array containing an array of polypeptides comprising that of SEQ. ID. NO.: 2, an immunogenic composition comprising a polypeptide of SEQ. ID. NO.:2, a screening assay for compounds binding to the polypeptide of SEQ. ID. NO.: 2 or the corresponding polynucleotides, a kit containing a corresponding polynucleotide or a specific antibody.

Inventions 4 to 1091 (Claims 3-6,8,9,11-30 partly)

-Idem as subject three but in reference to SEQ. ID. NO.: 3, 4, 6 to 73, 75 to 312, 314 to 402, 404 to 423, 425 to 524, 526 to 547, 549 to 575, 577 to 803, 805 to 1098.

Inventions 1092 to 1100 (Claims 4,6-14,16, 18-30 partly)

-Idem as subject 4 but in reference to SEQ. ID. NO.:5, 74, 313, 403, 424, 525, 548, 576, 804.

Invention 1101 (Claims 31 to 34)

-Computer readable medium and computer-based system for identifying fragments of the Bifidobacterium longum genome.

It should be noted that the above claims have as a subject matter computer readable medium and a computer based system which appear to constitute merely ways of presenting information and as such would not be regarded as patentable inventions in the sense of Art. 52.1 EPC. Subject matter excluded from patentability under Art. 52.1 EPC needs not be a subject of the search.

Invention 1102 (Claims 35 to 39)

-A strain of lactic acid bacterium and the uses thereof.

European Patent
Office**LACK OF UNITY OF INVENTION**
SHEET B

Application Number

EP 01 10 2050

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

The application has been divided into the above (groups of) inventions which individually are considered to meet the requirement of unity. If additional fees are paid for (one or more of) the, as yet, unsearched invention(s), the subsequent search(es) might reveal prior art which leads to a finding of lack of unity a posteriori within (one or more of) the, as yet, unsearched invention(s). Should this be the case, as a rule, no further invitation to pay additional fees will be issued. Only the first identified invention in each group of inventions, for which additional search fees have been paid in due time and which subsequently is considered to lack unity, will be searched.